

**Hormonal study to infertile women infected by *Toxoplasma gondii* parasite in different stage of disease in the Holy Karbala city**

دراسة هرمونية للنساء العقيمات المصابات بطفيلي التوكسوبلازما غوندي في مراحل مختلفة من المرض في مدينة كربلاء المقدسة

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**Abstract:**

This research on the impact of female infertility due to the parasite *Toxoplasma Gondi* infection on defended stage of disease and level of the thyroid hormones during the year 2014-2015 in the holy city of Karbala, where the study took 120 women suffering from infertility them 60 samples were positive to infected *T. gondii* parasite and 60 of infertile women non infected by parasite, collected the serum from all the samples and then examined in the laboratories of the Medical city of Karbala on injury parasite at various stages of the disease to the level of antibodies is different from (immunoglobulin G and immunoglobulin M) and then were examined thyroid hormone levels the hormone (thyroxine, triiodothyronine, and stimulation thyroid hormone) to them. The study showed that there is a relationship between antibodies to the parasite *Toxoplasma* in various stages of injury and age, where the distribution of antibodies to *Toxoplasma* serology positive in the relationship between age significantly in both cases that carry *Toxoplasma* IgM (severe cases) compared with IgG (chronic) in the level of the probability ( $P > 0.05$ ) moral value of (0.028, 0.019) also did not find a significant difference in other infections parasite carryover the results also showed that there are no relationship between thyroid hormone levels of thyroid with different age in the study groups, but nevertheless we see that there are relevant differences statistically significant differences in the level of a hormone (T3 (T4, TSH, and the level of antibodies moral value of (0.043, 0.036, 0.028), respectively, below the level of probability ( $P > 0.05$ ) when a chronic condition at a high level of immune globulin IgG *Toxoplasma* and the level of thyroid and low hormone in the control group. so were the recommendations to verify the level of hormones thyroid patients living with severe antibodies to *Toxoplasma* parasite to avoid the causes of the damage from the impact of the parasite in the body of patients.

**الخلاصة**

هذا البحث حول تأثير العقم عند النساء بسبب عدوى طفيلي التوكسوبلازما غوندي (*T. gondii*) على هرمونات الغدة الدرقية ومرحلة ومستوى الإصابة خلال العام 2014-2015 في مدينة كربلاء المقدسة، حيث اخذت الدراسة 120 امرأة يعانين من العقم منهن 60 عينة مصابة و60 عينة غير المصابة بطفيلي *T. gondii* من النساء العقيمات، حيث جمعت عينات من السيرم ثم فحصت في مختبرات المدينة الطبية كربلاء حول الإصابة بالطفيلي في مراحل مختلفة من المرض لمستوى الأجسام المضادة المختلف من (الغلوبولين المناعي جي و الغلوبولين المناعي ام) ثم تم فحص مستوى هرمون الغدة الدرقية

(هرمون الثيروكسين، ثلاثي يودوثيرونين، ومحفيز هرمون الغدة الدرقية) لها. اظهرت الدراسة ان هناك علاقة بين الأجسام المضادة لطفيلي التوكسوبلازما في مراحل مختلفة من الإصابة والعمر حيث توزيع أجسام مضادة لالتوكسوبلازما الأمصال إيجابية في العلاقة بين العمر بشكل ملحوظ في كل من الحالات التي تحمل التوكسوبلازما (IgM) (الحالات الشديدة) بالمقارنة مع (IgG) (حالة مزمنة) في مستوى احتمال ( $P > 0.05$ ) بقيمة معنوية (0.028، 0.019) كما لم نجد فرقا كبيرا في المرحل الأخرى من العدوى بالطفيلي كما بينت النتائج ان لا توجد علاقة بين مستويات هرمونات الغدة الدرقية مع اختلاف العمر في مجموعات الدراسة ولكن مع ذلك نحن نرى أن هناك فروق ذات دلالة إحصائية في مستوى هورمون ( $T_4$ , TSH,  $T_3$ ) ومستوى الأجسام المضادة بقيمة معنوية (0.043، 0.036، 0.028) على التوالي تحت مستوى احتمالية ( $P > 0.05$ ) عند الحالة مزمنة عند مستوى مرتفع من الغلوبولين المناعي IgG للتوكسوبلازما ومستوى هرمون الغدة الدرقية وانخفاض الهورمون في مجموعة السيطرة. لذا كانت التوصيات بالتحقق مستوى هورمونات الغدة الدرقية للمرضى الحاملين الأجسام المضادة الحاد لطفيلي التوكسوبلازما لتجنب أسباب الضرر من تأثير الطفيلي في جسم المرضى.

## **Introduction**

Toxoplasmosis is a zoonotic infection of animals caused by the protozoan parasite *Toxoplasma gondii*. It has the capacity to infect all warm-blooded animals, while the infection does not cause clinical symptom in the majority of animal species, in few cases it causes acute life-threatening disease, particular in sheep and goats, it may manifest itself as a disease of pregnancy by multiplying in the placenta and foetus (1). *Toxoplasma gondii* (Apicomplexan) is one of the most common parasitic protozoans in humans. The prevalence of *Toxoplasma* infection varies mostly from 20 to 80% in different territories. There are many cases for infect firstly from the consummation of raw or undercooked meat of an intermediate host (especially pigs, sheep and rabbits) containing tissue cysts, secondly from food or water contaminated with soil containing cat faces with oocysts (2). *Toxoplasma gondii* infects human beings in which appritaty are infected depend on (approximately 30% of the population depending on age and environment); However clinical symptoms are relatively uncommon pregnant women. Those particularly at risk of developing clinical illness include pregnant women, as the parasite can pose a serious threat to the unborn child if the mother becomes infected for the first time while pregnant, and individuals who are immunosuppressed, such as tissue transplant patients, AIDS patients, patients with certain types of cancer and those undergoing certain forms of cancer therapy (1). Thyroid gland is an essential gland in the body of human being that produces essential hormones regulated by the hypothalamic-pituitary-thyroid axis (3). The main function of thyroid gland is to secrete thyroxin to regulate basal metabolic related to mostly this hormone acts through nuclear receptors that are Tran scripted by numerous genes and these genes regulate a number of critical physiological functions in development and metabolism (4).  $T_3$ ,  $T_4$  and TSH determination are important factors in thyroid disease diagnosis.  $T_3$  determination is useful in monitoring both patients under treatment for hyperthyroidism, and the who have discontinued anti-thyroid drug therapy. It is especially valuable in distinguishing between thyroid and hyperthyroid subjects (5).

## **Objectives of the Study:**

- 1- To determine the prevalence of *Toxoplasma gondii* (IgG and IgM) in the sample of the study.
- 2- To find relationship between *Toxoplasma gondii* parasite (IgG/ IgM) and the study sample (case control).
- 3- To estimate the effect of *Toxoplasma gondii* parasite (IgG/IgM) on the thyroid hormones function ( $T_3$ ,  $T_4$ , TSH) in the patients woman.

## **Materials and methods**

### **Study period and location**

From 1st November 2014 to 30th June of 2015 a cross sectional study was carried on in Karbala city and private medical laboratories in Karbala, Iraq.

**Selection of patients and blood sampling :-**

Women patients suffering from infertility and disturbing from thyroid malfunction ,were referred to private laboratories by clinicians,were selected for the study .Atotal of 60 patiennnts aged between 15 and 45 years and above with an average age of 25 +-10 years were enrolled for the present study . prier collection the blood sample , a questionnaire given to each patient and complete information was obtained .We 10 ml of venous blood were collected to samples a sterile dry tube and kept for about 15 min to clot, then sera have been separated using centrifuge .the get sera were immediately tested for toxoplasmosis and thyroid functionality test . the serological tests were done using IgM and IgG ELISA bio-kits reagents manufactured by Barcelona –spain to detect anti – IgM and anti – IgG for *T.gondi* .The procedures used here were applied according to manufacturer guidelines according to thyroid hormones triiodothyronine (T<sub>3</sub>) ,Thyroxine (T<sub>4</sub>) and thyroid stimulation hormone (TSH).were determined using mini-videos machine which can measure hormones(6).

**Result:**

In study a correlation analysis of the three to thyroid function composite variables relationships, time of infection with *T.gondi* parasite and level of **Immunoglobulins** (IgG,IgM) and non-infected women normal case(control ) Sero-positive Toxoplasma antibody

Distribution in relation to age-. 120 cases **were studied** -(60 normal and 60 patient of women infected with Toxoplasmosis during eight months of study in Karbala city was in different age from (18-45) years to old (39-45) years old which showed in tables (1). we take the sample and no significant (p< 0.05). appears between the normal case and patient in deferent age contributed, as show in (Table 1, 2).

Table (1): Distribution of the study sample (case &control) according to age groups with comparison significant

Age groups (Years)	Status		Total	P-value & C.S.
	Case ( Infected, No.=60)	Control (Non- Infected, No.=60)		
	No. (%)	No. (%)		
18-24	6 (5.0)	9 (7.5)	15 (12.5)	$\chi^2 = 5.772$ P = 0.123 (NS)
25-31	34 (28.3)	25 (20.8)	59 (49.2)	
32-38	17 (14.2)	16 (13.3)	33 (27.5)	
39-45	3 (2.5)	10 (8.3)	13 (10.8)	
Total	60 (50.0)	60 (50.0)	120 (100.0)	
$\pm$ SD		$2.37 \pm 0.840 \bar{x}$		

No.,%:Percent,  $\bar{x}$ :Mean, SD: standard deviation,  $\chi^2$ : Chi-Square, P-value: Probability of chance, C.S.: Comparison significant, NS (Non significant): P>0.05.

Table (2): Distribution of the study sample (case & control) for *Toxoplasma gondii* parasite (IgG/ IgM) and thyroid function tests (T3, T4, TSH) with summary statistics

Variables	Groups	No.	$\bar{x}$	SD.	Min.	Max.
Ig	G	120	1.67	0.920	1	3
	M	120	1.55	0.887	1	3
Thyroid hormone function tests (Case)	T3	60	1.38	0.490	1	2
	T4	60	1.30	0.462	1	2
	TSH	60	1.25	0.437	1	2
Thyroid hormone function tests (Control)	T3	60	1.08	0.279	1	2
	T4	60	1.10	0.303	1	2
	TSH	60	1.07	0.252	1	2

No.: number,  $\bar{x}$ :Mean, SD.: standard deviation, Min.: Minimum, Max.: Maximum, IgG: Immunoglobulin G, IgM: Immunoglobulin M

In the present study there is a strong relationship between *Toxoplasma* antibodies distribution patients and normal case, the results observations which were summarized in table (3). Seropositive *Toxoplasma* antibody distribution in relation to age was significantly in both case which carry of *Toxoplasma* IgM (acute case) compared with IgG( chronic case ) ( $p=0.028$  , $p=0.019$  ) in Sequentially at  $P>0.05$ .but not deferent between them it showed in In table (4) .

Table (3): Distribution of the study sample (case control) and relationship between *Toxoplasma gondii* IgG according to age groups

Age groups (Years)	F	%	<i>Toxoplasma gondii</i> IgG			Total	P-v alue & C.S.
			Negative No. (%)	Equivocal No. (%)	Positive No. (%)		
18-24	15	12.5	10 (8.3)	1 (0.8)	4 (3.3)	15 (12.5)	$\chi^2= 15.178$ $P= 0.019$ (S)
25-31	59	49.2	29 (24.2)	4 (3.3)	26 (21.7)	59 (49.2)	
32-38	33	27.5	25 (20.8)	1 (0.8)	7 (5.8)	33 (27.5)	
39-45	13	10.8	13 (10.8)	- (0.0)	- (0.0)	13 (10.8)	
Total	120	100.0	77 (64.2)	6 (5.0)	37 (30.8)	120 (100.0)	

F: Frequency, %: Percent, No.: number, IgG: Immunoglobulin G,  $\chi^2$ : Chi-Square, P-value: Probability of chance, C.S.: Comparison significant, S (significant):  $P<0.05$ .

Table (4): Distribution of the study sample (case control) and relationship between *Toxoplasma gondii* IgM according to age groups

Age groups (Years)	F	%	<i>Toxoplasma gondii</i> IgM			Total	P-value & C.S.
			Negative No. (%)	Equivocal No. (%)	Positive No. (%)		
18-24	15	12.5	10 (8.3)	1 (0.8)	4 (3.3)	15 (12.5)	$\chi^2=14.13$ 2 P= 0.028 (S)
25-31	59	49.2	35 (29.2)	1 (0.8)	23 (19.2)	59 (49.2)	
32-38	33	27.5	30 (25.0)	- (0.0)	3 (2.5)	33 (27.5)	
39-45	13	10.8	11 (9.2)	- (0.0)	2 (1.7)	13 (10.8)	
Total	120	100.0	86 (71.7)	2 (1.7)	32 (26.7)	120 (100.0)	

F: Frequency, %: Percent, No.: number, IgM: Immunoglobulin M,  $\chi^2$ : Chi-Square, P-value: Probability of chance, C.S.: Comparison significant, S (signify ant): P<0.05.

The results showed in table (5) Which appears that no relationship between level of thyroid hormone with age in deferent study group and non-significantly in the level of hormone in patient infected with Toxoplasmosis. But there is significantly P>0.05 in level— antibody (IgG, IgM). Showed in table (6), there is significant in level of hormone T3 and T4 and TSH (0.043, 0.036, and 0.028) in chronic case when IgG level of toxoplasma is elevated the level of thyroid hormone decrease control with normal case.

Table (5): Relationship between thyroid hormones function tests (T3, T4, TSH) and *Toxoplasma gondii* (IgG / IgM) relative to Infected women only (case) among the study sample

Status	Age groups (Years)	T3		T4		TSH		P-value & C.S.
		Normal No. (%)	Abnormal No. (%)	Normal No. (%)	Abnormal No. (%)	Normal No. (%)	Abnormal No. (%)	
Infected	18-24 Count % of Total	4 (6.7)	3 (5.0)	3 (5.0)	4 (6.7)	5 (8.3)	2 (3.3)	T3= 0.073 (NS) T4= 0.157 (NS) TSH= 0.830 (NS)
	25-31 Count % of Total	24 (40.0)	9 (15.0)	26 (43.3)	7 (11.7)	24 (40.0)	9 (15.0)	
	32-38 Count % of Total	7 (11.7)	11 (18.3)	11 (18.3)	7 (11.7)	14 (23.3)	4 (6.7)	
	39-45 Count % of Total	2 (3.3)	- (0.0)	2 (3.3)	- (0.0)	2 (3.3)	- (0.0)	
	Total Count % of Total	37 (61.7)	23 (38.3)	42 (70.0)	18 (30.0)	45 (75.0)	15 (25.0)	
Non-Infected	18-24 Count % of Total	9 (15.0)	- (0.0)	9 (15.0)	- (0.0)	7 (11.7)	2 (3.3)	T3= 0.064 (NS) T4= 0.180 (NS) TSH= 0.143 (NS)
	25-31 Count % of Total	20 (33.3)	5 (8.3)	21 (35.0)	4 (6.7)	23 (38.3)	2 (3.3)	
	32-38 Count % of Total	16 (26.7)	- (0.0)	16 (26.7)	- (0.0)	16 (26.7)	- (0.0)	
	39-45 Count % of Total	10 (16.7)	- (0.0)	8 (13.3)	2 (3.3)	10 (16.7)	- (0.0)	
	Total Count % of Total	55 (91.7)	5 (8.3)	54 (90.0)	6 (10.0)	56 (93.3)	4 (6.7)	

IgG: Immunoglobulin G, IgM: Immunoglobulin M, No.: number, %: Percent, P-value: Probability of chance, C.S.: Comparison significant, S (significant): P<0.05, NS (Non-significant): P>0.05.

Table (6): Relationship between thyroid hormones function tests (T3, T4, and TSH) with infected / Non-infected women among the study sample (case &control) according to age groups.

<i>Toxoplasma gondii</i> parasite	Groups	T3		T4		TSH		P-value & C.S.
		Normal No.(%)	Abnor mal No. (%)	Normal No. (%)	Abnor mal No. (%)	Normal No. (%)	Abnor mal No. (%)	
IgG	Negative Count % of Total	7 (11.7)	10 (16.7)	12 (20.0)	5 (8.3)	15 (25.0)	2 (3.3)	T3= 0.043 (S) T4= 0.036 (S) TSH= 0.028 (S)
	Equivocal Count % of Total	5 (8.3)	1 (1.7)	4 (6.7)	2 (3.3)	2 (3.3)	4 (6.7)	
	Positive Count % of Total	25 (41.7)	12 (20.0)	26 (43.3)	11 (18.3)	28 (46.7)	9 (15.0)	
	Total Count % of Total	37 (61.7)	23 (38.3)	42 (70.0)	18 (30.0)	45 (75.0)	15 (25.0)	
IgM	Negative Count % of Total	18 (30.0)	8 (13.3)	21 (35.0)	5 (8.3)	20 (33.3)	6 (10.0)	T3= 0.565 (NS) T4= 0.263 (NS) TSH= 0.643 (NS)
	Equivocal Count % of Total	1 (1.7)	1 (1.7)	1 (1.7)	1 (1.7)	2 (3.3)	- (0.0)	
	Positive Count % of Total	18 (30.0)	14 (23.3)	20 (33.3)	12 (20.0)	23 (38.3)	9 (15.0)	
	Total Count % of Total	37 (61.7)	23 (38.3)	42 (70.0)	18 (30.0)	45 (75.0)	15 (25.0)	

No.: number, %: Percent, P-value: Probability of chance, C.S.: Comparison significant, NS (Non significant): P>0.05

**Dissection**

*T. gondii* is one of **the** tissue apicomplexan protozoa, where the sluggish (bradyzoites) released from the cysts in parasitized tissues to form active or proliferative Tachyzoites that dwells in the circulated blood and reach other organs including brain, eyes, muscular fibres and Thyroid gland. **So** it **can** effect on physiological of body according to which organs infected by cyst formation and tissue Changes such as level of Thyroid gland hormonal (7). In this study tack side of relationship between time of infection with *T. gondii* in body and type immunoglobulins (IgM, IgG) (acute or chronic) on the and function of thyroid hormone by test the levels of the (T3,T4,TSH) hormone and study relationship between patient age arrange between 18-45 old years to 39-45 years old which showed no significant (p<0.05 ). appears between the normal case and patients . In study used mini-Vedas machine for thyroid function elements test (T3,T4,TSH).and Elisa used to detected Sero-positive Toxoplasma antibody .

the study showed significantly in P value 0.05 in both case which carry of *Toxoplasma* antibody in immunoglobulin IgM (acute case) Compared with immunoglobulin IgG antibody (Chronic case) ( $p=0.028$  , $p=0.019$  ) in Sequentially significant ( $p<0.05$ ).but not significantly deferent between them and no relationship between level of thyroid hormone with age in deferent study group and non-significantly in the level of hormone in patient infected with Toxoplasmosis . But the study appears there is significantly in level antibody (IgG, IgM). There is significant decrease in level of hormone T3 and T4 and TSH (0.043, 0.036, 0.028) significant ( $p<0.05$ ). in chronic case when IgG level of *toxoplasma* is elevated the level of thyroid hormone decrease control with normal case it agree with The results in this regard were in agreement with those recorded by (9,10). In study- showing the exploring the relation between Toxoplasma infection and thyroid hormones, on other hand the relation between Toxoplasma infection changes in acute chase (IgM) and chronic (IgG) Concerning frequency of Toxoplasma antibodies according to the age group, in spite of the statistical analysis appears that non-significantly but significantly in decrease level of Thyroid hormone in Toxoplasma IgG antibodies (chronic case) on the other. (11) ,there showing that in there studied the Latent toxoplasmosis was associated with infected Women with latent toxoplasmosis had lower TSH levels than the Toxoplasma-negative ones There are found the latent toxoplasmosis was associated with decrease in serum we found a positive correlation between FT4 and the index of positivity for anti-Toxoplasma IgG antibodies. Our study we demonstrate that the infection is not associated with hypothyroidism ,as could be expected as a result of the promotion of thyroid autoimmunity ,but it is associated with a slight decrease in TSH ,and an increase in FT4 in chronic case when IgG antibody is higher and it discuss that correlation with HGG hormone which is Known to have a TSH-like factor in pregnancy transitory gestation hyperthyroidism (12) Our date thus indicate that latent toxoplasmosis per se might have a moderate stimulatory effect on thyroid hormone production in pregnancy and Our study agree with Studies in Nyla female mice infected with *T. gondii*, exhibited hypogonadotropic hypogonadism secondary to hypothalamic dysfunction (13)(14).

In mice infected with *T. gondii* Cornell strain, present atrophy in the thymus, ovaries, and uterus, cessation of cycling, anovulation, and decline of serum thyroxine T4) levels(13).another study discus the decrease the level of thyroid hormone due to There are different modes of changes in the serum level of Cu, Zn, and Mg in

Patients as compared with normal controls and these modes are explained according to the immunity response. Zinc deficiency affects the biological activity of thymus hormones and has a major effect on cell mediated immunity perhaps as a result

(15, 16, 17). Zinc is the most important trace elements for immune function and its deficiency is associated with immune abnormalities and increase susceptibility to infectious diseases. The effect of zinc added diet on cellular immunity in toxoplasmosis was investigated in rats and found that zinc diet in toxoplasmosis stimulated the

Cellular immunity increased CD8 the total lymphocytes (18). In stress, which is present in women with frequent abortion, the decrease of zinc reflects an apparent zinc deficiency because of redistribution of serum zinc into the liver and because of decrease in serum albumin concentration where over 70% of the serum zinc is bound to albumin (19). But study of Our study demonstrated that there is no significant correlation between these hormones levels in and their complication the almost widespread parasite diseases common between human and warm-blood animals, which is widely distributed around the world.it dis agree with result of they showed that increase in TSH in both meal and female and increase the level of T3and T4 in female all infected with *T.gondi* they do not analyses according time of infection. (20)



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