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Original Research Article

The relationship between people with toxoplasmosis and changes in thyroid hormone levels between 2017 and 2018, Khartoum, Sudan

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Abstract

***Toxoplasma gondii* parasites are capable to affect any organs and glands in human and this causes the appearance of different clinical sign. The present study was performed to examine the effect of toxoplasmosis infection on thyroid hormone levels among Sudanese patients in Khartoum State that help in early diagnosis and treatment and there is no data in Sudan. The study was cross section design which was conducted among 100 patients including males and females (pregnant and non pregnant) with toxoplasmosis. Enzyme Linked Immunosorbent Assay (ELISA) was used to detect the presence of anti *Toxoplasma* IgM and IgG antibodies and detect the levels of thyroid hormones. The study showed *Toxoplasma* antibody types in relation to patient gender, especially 61.1% of IgG was critical to females including pregnant and non pregnant and 38.8% of the same type of antibodies within males and 6.6 % of IgM was critical to females including pregnant and non pregnant. Also 2.2% of the same type of antibodies within males and 54.4% was abnormal thyroid hormones levels. 34.4% was critical to females including pregnant and non pregnant and 20.0% in males. The prevalence of abnormal biochemical thyroid function reported here was substantial. A thyroid function hormones level assessed by using ELISA technique among patients with toxoplasmosis is useful.**

Keywords: *Toxoplasma gondii*, Thyroid hormones, Sudanese Patients, ELISA

INTRODUCTION

Toxoplasma gondii (*T.gondii*) is an intracellular protozoan parasite with wide spread distribution. *T.gondii* has a large variety of host, including humans and most worm-blood species, but it completes it's sexual cycle and produces oocysts only in the intestinal tract of felids (Montoya and Liesenfeld, 2004). Human acquire *T.gondii* infection through oral ingestion of food or water contaminated with oocysts from cat faces, ingestion of cyst contained in raw or under cooked meat, trans-placental transmission of tachyzoites from infected mother to her fetus and tachyzoites and tissue cyst acquisition via solid organ transplantation (Alvarados *et al*., 2011). Although clinical presentation of toxoplasmosis is benign in an immune-competent population, toxoplasmic encephalitis due to reactivation of a latent infection may lead to severe cerebral lesions in acquired

immunodeficiency syndrome (ADIS) patients (Assis *et al*., 2004). In pregnant women, when infection is transmitted to the fetus, it may lead to mental retardation, blindness, epilepsy and death (Montoya and Liesenfeld, 2004). The severity of the outcomes of newborns depends on the gestational stage during pregnancy when the infection occurred. Early maternal infection can cause more significant congenital toxoplasmosis in new borne (Paquet and Yudin, 2013). The detection of *T.gondii* itself is very difficult, hence the diagnosis of human toxoplasmosis is typically based on serological detection of antibodies by using latex agglutination test (LAT), enzyme- linked immunosorbent assay (ELISA), indirect fluorescent antibody test (IFAT) and complement fixation (CFT). Latex agglutination test is better adapted for developing countries where rural districts often take the equipment needed for ELISA (Chuang *et al*., 2014). Molecular biology and histological demonstration of *T.gondii* is the main laboratory diagnostic tools and isolation of the organism, other rarely methods include demonstration of antigen in serum and body fluids, *Toxoplasma* in skin test and antigen- lymphocyte transformation (Ivovic *et al*., 2012).

Thyroxine (T4) a form of thyroid hormones is the major hormone secreted by the follicular cells of the thyroid gland. T4 is transported in blood, with 99.95% of the secreted T4 being protein bound, principally to thyroxine-binding globulin (TBG), and, to a lesser extent, to transthyretin and serum albumin. T4 is converted in the tissues by deiodinases to T3. The half-life of thyroxine once released into the blood circulatory system is about 1 week. Triiodothyronine (T3) is a thyroid hormone. Thyroid-stimulating hormone (TSH) activates the production of thyroxine (T4) and T3. This process is under regulation. The thyroid gland releases greater amounts of T4 than T3, so plasma concentrations of T4 are 40-fold higher than those of T3. Most of the circulating T3 is formed peripherally by deiodination of T4 (85%). This thyroid hormone is similar to thyroxine but with one fewer iodine atoms per molecule. In addition, T3 exhibits greater activity and is produced in smaller quantity. TSH is a glycoprotein which consists of two subunits, the alpha and the beta subunit. TSH production is controlled by a Thyrotropin Releasing Hormone, (TRH). The levels of thyroid hormones (T3 and T4) in the blood have an effect on the pituitary release of TSH. When the levels of T3 and T4 are low, the production of TSH is increased, and conversely, when levels of T3 and T4 are high, then TSH production is decreased. This effect creates a regulatory negative feedback loop **(**Demers *et al*., 2002).

This work was conducted to determine the effect of *Toxoplasma gondii* infection on thyroid hormones levels among Sudanese patients in Khartoum State, to estimate thyroid stimulating hormone (TSH) level in patients affected with toxoplasmosis using enzyme linked immune sorbent assay (ELISA), to estimate thyroxin (T4) level in patients affected with toxoplasmosis using enzyme linked immune sorbent assay (ELISA), to estimate triiodothyronine (T3) level in patients affected with toxoplasmosis by enzyme linked immune sorbent assay (ELISA) and to correlate between abnormal thyroid hormones levels and *Toxoplasma gondii* infection according to gender males and females sub group (pregnant and non pregnant).

MATERIALS AND METHODS

Study design

A cross-section study design was applied to detect the effect of *Toxoplasma gondii* infection on thyroid hormones levels among Sudanese patients in Khartoum State- Sudan.

Study area

The study was applied in Khartoum state and specimens were received from the entire parts of Khartoum, dealing with two advanced laboratories.

Study period

Blood samples collection were started on October 2015 to February 2016.

Inclusion and exclusion criteria

This study included 100 patients with toxoplasmosis, males and females with different age and exclude patient with toxoplasmosis known with thyroid disease before the discovery infection with *Toxoplasma gondii*.

Data analysis

The data obtained from this study was analyzed and interpreted by statistical package for social sciences (SPSS). ANOVA test, t-test and correlation coefficient (rho) were used. *P.* value less than 0.05 considered significant. Then data was presented in tables and figures.

Materials Laboratory kits

Table of laboratory kits used in this study

Kit	Company	Origin
Thyrotropin (TSH) Hormone Enzyme Immunoassay Test Kit	Roche diagnosis (Cobas)	Germany
Thyroxin (T4) Hormone Enzyme Immunoassay Test Kit	Roche diagnosis (Cobas)	Germany
Triiodothyronine (T3) Hormone Enzyme Immunoassay Test Kit	Roche diagnosis (Cobas)	Germany

Methods

Detection of anti- *Toxoplasma gondii* antibody (IgG) by ELISA technique

Principle

In 1st incubation: 10 Micro\L sample of biotinylated recombinant *T.gondii* antigen; and a *T.gondii*-specific recombinant antigen labeled with a ruthenium complex form a sandwich complex. In 2nd incubation: after addition of streptavidin-coated microparticles; the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture was aspirated into the measuring cell where the micro particles were magnetically captured into the surface of the electrode. Unbound substances are then removed with pro cell. Application of a voltage to the electrode then induced chemiluminescent emission which is measured by a photomultiplier. Results are determined automatically by the elecsys software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by toxo IgG calibration.

Calculation

The analyzer automatically calculates the analyte concentration of each sample in IU\ml.

Interpretation of results

Non reactive: < 1 IU\ml
Indeterminate: ≥ 1 _ < 3 IU\ml
Reactive: ≥ 3 IU\ml

Detection of anti-*Toxoplasma gondii* antibody (IgM) by ELISA technique:

The same principle, assay procedure of ELISA-IgG technique was adopted in ELISA-IgM detection with few exception, the specific antibody IgM was used instead of IgG specific antibody.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of Cal 1 and Cal 2.

Interpretation of results

Non reactive: < 0.8 col
Indeterminate: ≥ 0.8 _ < 1.0 col
Reactive: ≥ 1.0 col

Thyroid hormones analysis

Principle

The principle of thyroid hormones (T4, T3, TSH) same as principle of ELISA-IgG technique was adopted in ELISA-thyroid hormones detection with few exception, the specific antibody of (T4 or T3 or TSH) was used instead of IgG specific antibody.

Determination of serum T4 levels

Table showed Precicontrol universal

Value	Range	1SD	Unit
12.2	9.64-14.8	0.85	µ g\dl

Determination of serum T3 levels

Table showed Precicontrol universal

Value	Range	1SD	Unit
3.73	2.83-4.63	0.30	n g\ml

Determination of serum TSH levels

Table showed Precicontrol universal

Value	Range	1SD	Unit
0.17	0.139-0.201	0.010	µ l U\ml

Ethical consideration

Declaration letter from research committee of the community department at Elzaeem Elazhari University

Table 1. Mean and SD levels of Thyroid hormones in test and control group

		Mean± Std. Deviation	Minimum- Maximum	P.value
TSH	Case	0.22304± 0.203362	0.103-2.000	0.335
	Control	0.16040±0.016834	0.139-0.190	
T4	Case	10.30800±3.364219	0.405-19.400	0.537
	Control	9.64394±0.734662	9.630-11.700	
T3	Case	3.72300±1.240359	1.500-7.110	0.159
	Control	3.15900±0.524533	3.150-4.450	

Table 2. Mean and SD levels of TSH between males and females among test and control group

Study groups			Mean± Std. Deviation	Minimum-maximum	P.value
Case	TSH	Males	0.26371±0.309687	0.139-2.000	0.131
		Females	0.19716±0.077596	0.103-0.422	
Control	TSH	Males	0.15700±0.008185	0.150-0.166	
		Females	0.16186±0.019861	0 .139-0.190	

Table 3. Mean and SD levels of T4 between males and females among test and control group

Study groups			Mean± Std. Deviation	Minimum-maximum	P.value
Case	T4	Males	8.67271±2.606044	0.405-13.500	0.028
		Females	10.26200±3.657475	5.210-19.400	
Control	T4	Males	6.62667±0.576855	5.880-7.200	
		Females	7.17143±0.664426	5.630-9.700	

Table 4. Mean and SD levels of T3 between males and females among test and control group

Study groups			Mean± Std. Deviation	Minimum-maximum	P.value
Case	T3	Males	2.95829±1.158949	1.500-7.110	0.223
		Females	3.28673±1.283447	1.500-6.700	
Control	T3	Males	3.90333±0.667108	3.160-4.450	
		Females	3.64571±0.491048	3.150-4.200	

was obtained. Also, consent was obtained from the patients and confidentiality of human subject data was ensured.

RESULTS

The results showed that the difference in mean of TSH, T4 and T3 between test and control group was found to be statistically insignificant (Table 1). The results showed that the difference of mean of TSH between males and females among test and control groups was found to be statistically insignificant (P= 0.131) (Table 2). The results showed statistics and significant mean differences of T4 between males and females among test and control groups (P= 0.028) (Table 3). The result showed statistics and insignificant mean differences of T3 between males and females among test and control groups (P= 0.223) (Table 4). The results showed statistics and insignificant mean differences of IgG titer between males and females among test and control groups (P= 0.982) (Table 5). The results showed statistics and insignificant mean differences of IgM titer between males and females among test and control groups (P= 0.346) (Table 6). The results showed statistics and insignificant mean differences of TSH between males and females subgroup among test and control groups (P= 0.121) (Table 7). The results showed statistics and significant mean differences of T4 between males and females subgroup among test and control groups (P= 0.000) (Table 8). The results showed statistics and significant mean differences of T3 between males and females subgroup among test and control groups (P= 0.000) (Table 9). The result showed statistics and insignificant mean differences of IgG titer

Table 5. Mean and SD levels of IgG titer between males and females among test and control group

Study groups			Mean± Std. Deviation	Minimum- maximum	P.value
Case	IgG titer	Males	3.94286±0.525405	3.500-5.000	0.982
		Females	4.74545±0.515255	3.000-6.000	
Control	IgG titer	Males	1.00000±0.000000	1.000-1.000	
		Females	0.92857±0.345033	0.500-1.500	

Table 6. Mean and SD levels of IgM titer between males and females among test and control group

Study groups			Mean± Std. Deviation	Minimum- maximum	P.value
Case	IgM titer	Males	0.50286±0.385384	0.100-2.000	0.346
		Females	0.60909±0.587295	0.100-3.000	
Control	IgM titer	Males	0.33333±0.208167	0.100-0.500	
		Females	0.37143±0.262769	0.100-0.700	

Table 7. Mean and SD levels of TSH between males and females subgroups among test and control group

Study groups			Mean± Std. Deviation	Minimum-Maximum	P.value
Case	TSH	Males	0.26371±0.309687	0.13 - 2.000	0.121
		Females (non pregnant)	0.22050±0.077504	0.139 - 0.422	
		Females (pregnant)	0.13493±0.028037	0.103-0.190	
Control	TSH	Males	0.15700±0.008185	0.15 0- 0.166	
		Females (non pregnant)	0.16550±0.021517	0.139 - 0.190	
		Females (pregnant)	0.1700±0.020664	0.120 - 0.180	

Table 8. Mean and SD levels of T4 between males and females subgroups among test and control group

Study groups			Mean± Std. Deviation	Minimum-Maximum	P.value
Case	T4	Males	8.67271±2.606044	0.405-13.500	0.000
		Females (non pregnant)	8.62675±2.197247	5.210-13.500	
		Females (pregnant)	14.62267±3.183483	9.640-19.400	
Control	T4	Males	6.62667±.676855	5.880-8.200	
		Females (non pregnant)	8.62675±2.197247	6.630-9.700	
		Females (pregnant)	7.11667±.510718	6.750-9.700	

Table 9. Mean and SD levels of T3 between males and females subgroups among test and control group

Study groups			Mean± Std. Deviation	Minimum-Maximum	P.value
Case	T3	Males	2.95829±1.158949	1.500-7.110	0.000
		Females (non pregnant)	2.79025±0.902312	1.500-4.500	
		Females (pregnant)	4.61067±1.226100	2.900-6.700	
Control	T3	Males	3.90333±0.667108	3.160-4.450	
		Females (non pregnant)	3.48000±0.484355	3.150-4.200	
		Females (pregnant)	3.86667±0.493288	3.300-4.200	

Table 10. Mean and SD levels of IgG titer between males and females subgroups among test and control group

Study groups		Mean± Std. Deviation	Minimum-Maximum	P.value
Case IgG Titer	Males	3.94286±0.525405	3.500-5.000	
	Females (non pregnant)	4.15000±0.450071	3.500-5.000	
	Females (pregnant)	3.83333±0.677882	3.000-5.000	0.994
Control IgG Titer	Males	1.00000±0.000000	1.000-1.000	
	Females (non pregnant)	1.00000±0.408248	0.500-1.500	
	Females (pregnant)	0.83333±0.288675	0.500-1.000	

Table 11. Mean and SD levels of IgM titer between males and females subgroups among test and control group

Study groups		Mean± Std. Deviation	Minimum-Maximum	P.value
Case IgM Titer	Males	0.50286±0.385384	0.100-2.000	
	Females (non pregnant)	0.60750±0.618678	0.100-3.000	
	Females (pregnant)	0.61333±0.513902	0.100-2.000	0.643
Control IgM Titer	Males	0.33333±0.208167	0.100-0.500	
		0.47500±0.262996	0.100-0.700	
	Females (non pregnant)	0.23333±0.230940	0.100-0.500	
	Females (pregnant)			

Table 12. Correlations between IgG and IgM titer with TSH in case group

Study groups			TSH
Case	IgG titer	R value	0.019
		P value	0.862
	IgM titer	R value	0.294
		P value	0.005

Table 13. Correlations between IgG and IgM titer with T4 in case group

Study groups			T4
Case	IgG titer	R value	0.053
		P value	0.622
	IgM titer	R value	-0.084
		P value	0.429

Table 14. Correlations between IgG and IgM titer with T3 in case group

Study groups			T3
Case	IgG titer	R value	-0.011
		P value	0.918
	IgM titer	R value	0.040
		P value	0.707

between males and females subgroup among test and control groups (P= 0.994) (Table 10). The result showed statistics and insignificant mean differences of IgM titer between males and females subgroup among test and control groups (P= 0.643) (Table 11). The results showed that there was a positive relation between IgG titer and TSH (R value .019), the result statistically was found to be insignificant at P= 0.862 also positive relation between

IgM titer and TSH (R value .294), the result statistically was found to be significant at P=.005; implied that when the IgG and IgM titer was high the TSH was high (Table 12). The results showed that there was a positive relation between IgG titer and T4 (R value .053), the result statistically was found to be insignificant at P= .622; implied that when the IgG titer was high the T4 was high. And negative relation between IgM titer and T4 (R value -.084), the result statistically was found to be insignificant at P=.429; showing that when IgM was low the T4 was high (Table 13). The results showed that there was negative relation between IgG titer and T3 (R value -.011), the result statistically was found to be insignificant at P=.918; showing that when IgG was low the T3 was high and a positive relation between IgM titer and T3 (R value .040), the result statistically was found to be insignificant at P= .707; implied that when the IgM titer was high the T4 was high (Table 14).

DISCUSSION

Abnormal thyroid function has multiple implications for public health. However, the magnitude of the problem is not entirely known, nor is the exact relationships to other health problems which are well delineated; the overall 54.4% of abnormal levels of three hormones, 34.4% was critical to females including pregnant and non-pregnant and 20.0% in males. Considered in this study, it was very high because the size of the samples, 100 was not too large and not comprehensive to all populations of Khartoum city. The reasons for this high rate may be attributed to the type of nutrition, poverty, poor hygienic condition and absence of health programs concerning endocrinology in general and thyroid in particular; in addition to genetic disorders (Al-Terihy *et al*., 2012). This study represented the first study in Sudan according to internet based research in scholar database about the possible effect of *T.gondii* on TSH, T3 and T4 serum levels among toxoplasmosis infected Sudanese patients. For this reason, there was no available data to compare with. In current study, the TSH was high in (49.9%). These findings come in contrary with previous study was done in Brazil by Castillo *et al.* (2006), indicating normal serum level of TSH in all infected cases even with sub-acute thyroiditis. The current results come in accordance with previous study by Stahl and Kaneda (1998) indicating that after experimental inoculation of *T.gondii* in a murine model there was depression in TSH production. This gives an indication that during the reactivation or seroconversion from latency had severe damage on the tissue (including thyroid gland). In such patients, especially cysts formation in the cervical lymphatic glands and thyroid gland may involve with highly parasitaemia or due to rupture of the cyst during trauma, leading to the release of trophozoites with parasite disposal product that may reach hypothalamus and alter its stimulation; therefore disturbance in TSH secretion and abnormal outcomes of T3 and T4 productions is resulted (Ain *et al*., 1987). Regarding increase of serum level of T4 (43.6%) in the present study come in line with Tozzoli *et al*. (2008) in Italy and a other clinical study of canine toxoplasmosis in Brazil by Castillo *et al.* (2006), indicating normal serum level of T4 in 50% of infected cases, T4 was increased in (37.5%) with significant correlation between anti-*Toxoplasma* antibodies and serum level of T4. Decrease serum level of T4 has not been detected in all positive cases, instead in (12.5%) of positive cases in canine model have low serum levels of T4 (Castillo *et al*., 2006). In other study of murine toxoplasmosis, a decline in T4 level was detected Stahl and Kaneda (1998). Which in turn reflect the decline in T3 serum level as T4 a pro-hormone for T3 and the ratio of T4 to T3 released into the blood was roughly 20 to 1 in serum, which gives possibility of hypothalamic dysfunction. Increased serum level of T4, T3 reflects the fact that *T.gondii* may initiates the development of a state of hypothyroidism even. This may be due to direct involvement of thyroid gland by *T.gondii*, multiplication in thyroid tissue and subsequent alteration of thyroid hormones (Gillespie and Pearson, 2001). Also may be due to reactivation of latent toxoplasmosis which may persist after or within 6 months of recovery from first initiation of toxoplasmosis (Salman, 2007).

CONCLUSION

The prevalence of abnormal biochemical thyroid function reported here was substantial. A thyroid function hormones level assessed by using ELISA technique among patients with toxoplasmosis was useful.

RECOMMENDATIONS

From the results of this preliminary study about some thyroid function tests in relation to toxoplasmosis: Highly recommended to interested researchers to carry on further studies with large size of patients. And assess all elements in thyroid tests in order to obtain obvious explanation about the role of infectious agents in sub-acute thyrotoxicosis.

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REFERENCES

Ain KB, Mori Y, Refetoff S (1987). Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for

estrogen-induced elevation of serum TBG concentration. *J. Clin. Endocrinol. Metab.* **65**: 689.

Al-Terihy FA, Shemran K, Abdulsamie Alta'ee AH, Jabuk Sh. K (2012). The association between thyroid hormones and lipid profile in patients with primary hyperthyroidism. *Med. J. Babylon*, **9** (4): 721-727.

Alvarados EC, Estrada MS, Liesenfeld O (2011). *T.gondii* infection in workers occupationally exposed to un washed raw fruits and vegetables: a case control seroprevalence study. *Parasit Vector*, 4:235.

Assis AM, Barreto ML, Gomes GS, Prado MS, Santos NS, Santos LM (2004). Childhood anemia prevalence and associated factors in Salvador, Bahia, Brazil. *Gad Saude Publica*, **20**:1633-1641.

Castillo VA, Gmbaro G, Vernica S (2006). Toxoplasmosis as a cause of sub-acute thyroiditis in dogs. *Redvet*, **7**(3):1-11.

Chuang TW, Lin HS, Wu CH, Liu YC, Langinlur MK (2014). *T.gondii* infection seroprevalence and associated risk factors among primary school children in the Capital area of the Republic of the Marshall Islands. *JPNJ Infect Dis*, **67**: 405-410.

Demers L, Carole M, Spencer A (2002). "LMPG: Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease", National Academy of Clinical Biochemistry (USA).

Gillespie SH, Pearson RD (2001). Principles and Practice of Clinical Parasitology. 1st edition. New York, Wiley Online Library.

Ivovic V, Vujanic M, Zivkovic T, KLun I, Djurkovic- Djakovic O (2012). Molecular detection and geno-typing of *T.gondii* from clinical samples. *Toxoplasmosis-Recent Advances*: 103-120.

Montoya JG, Liesenfeld Q (2004). Toxoplasmosis. *Lancet*, **363**: 1965-1976.

Paquet C, Yudin MH (2013). Toxoplasmosis in pregnancy, prevention, screening and treatment. *Job stet Gynaecol*, **53**: 78-81.

Salman Y (2007). Serological Cross Reaction among Some Causative Agents of Women Abortions (Toxoplasma gondii & Cytomegalovirus & Rubella Virus), with the Incidence of Hepatitis Virus (B &C). *Tik J Pharm Sci*, **3**:102-11.

Stahl W, Kaneda Y (1998). Aetiology of thyroidal dysfunction in murine toxoplasmosis. *Parasitology*,**117** (03):223- 27.

Tozzoli R, Barzilai O, Ram M, Villaita D, Bizzaro N (2008). Infection and autoimmune thyroid diseases: parallel detection of antibodies against pathogens with proteomic technology. *Autoimmun Rev*, **8**:112-115.