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ORIGINAL ARTICLE

Seroprevalence of *Toxoplasma gondii* and Its Effect on the Levels of Dopamine and Adrenaline in Humans

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ABSTRACT: The current study was conducted in Maysan province, Southern Iraq. Blood samples were collected from 174 individuals (male and female), from December 2020 to May 2021. ELISA was used to calculate the seroprevalence of *Toxoplasma gondii* by determining the levels of anti-toxoplasma IgM and IgG, as well as the levels of dopamine and adrenaline in the participants' blood. The overall seroprevalence of toxoplasmosis in Amarah city is 52.3%. In regards to the seropositive cases, there is 32.97% positive to IgM, 38.46% is positive IgG, and 28.57% is positive to both IgM + IgG. The level mean of dopamine in toxoplasmosis-seropositive cases is $2.9543x10^{-2}$ mg ml^{-1}, which is higher than that of negative cases ($1.8086x10^{-2}$ mg ml^{-1}). There are statistically significant differences ($p<0.05$) between the levels of dopamine in toxoplasmosis-seropositive and negative cases. The mean level of adrenaline in toxoplasmosis-seropositive cases is $2.8752x10^{-2}$ mg ml^{-1}. Which is higher than that of negative cases ($1.3670x10^{-2}$ mg ml^{-1}), there is a statistically significant difference ($p<0.05$) between its levels in toxoplasmosis-seropositive and negative cases.

INTRODUCTION

Toxoplasma gondii (*T. gondii*) is one of the most worldwide parasites; it can infect and reproduce in nucleated cells [1] of approximately 350 species of warm-blooded animals such as birds, livestock, humans, and other vertebrates, as intermediate hosts [2]. Although it infects about 2.3 billion individuals of the global population [3], *T. gondii* is still considered one of the neglected diseases in the world [4, 5]. It is a foodborne disease [6], where human obtained the infection by ingesting mature oocysts which were excreted with feces of infected cats (as the definitive host) and contaminated foods such as vegetables, fruits, meat and water, or contaminated the soil [7, 8]. Transmission of *T. gondii* to the fetus is frequently related to the infection acquired during pregnancy, resulting in congenital defects [9].

The world regions vary in the infection rates of *Toxoplasma gondii* depending on the variation in nutrition behavior, hygiene, geographic-environmental conditions and socio-demographic factors [10, 11]. The global seroprevalence of toxoplasmosis ranged between 0.2 - 100% [12 – 17].

Retinitis, intracerebral calcification, psychopathy, and hydrocephalopathy are the main signs of congenital toxoplasmosis [18].

Since the 1980s, the ability of *Toxoplasma gondii* to induce an immune response had been known, and the IgM was the first antibody to face the invasion of this parasite at the acute phase [19]. It was also detected that IgG in the blood of toxoplasmosis chronic infections [20, 21]. IgM creates during the first week of infection [22] and reached its highest level within the three weeks after the invasion, then it gradually decreases over time, which

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coincides with the emergence of IgG which usually appears through the second week after infection and reach its maximum level within 8 to 10 weeks of infection. Therefore, the presence of IgM only can be employed to approve that the infection is acute, while the presence of IgG only is an indicator of a chronic or previous infection [23, 24].

Some serological methods were evolved to diagnose *T. gondii* [23]. The enzyme-linked immunosorbent assay (ELISA) is classified as the gold standard immunoassay and is extremely sensitive for use in detecting and measuring substances, such as antibodies, antigens, proteins, glycoproteins, hormones, ….ect [25, 26]. This method is widely used in the investigation of anti-*Toxoplasma* IgG and IgM immunoglobulins.

Dopamine is a neurotransmitter between neurons, affecting the motivational aspect of reward-driven behavior. When human expect a reward, the majority of stimuli increase dopamine levels in the brain [27]. This neurotransmitter is important in the reward system, low levels of dopamine have been induced to Parkinson's disease, and high amounts of dopamine have been linked to schizophrenia [28].

Adrenaline is a hormone and a neurotransmitter [29] it is secreted by the medulla of the adrenal gland as well as some of the central nervous system's neurons [30]; it is a chemical neurotransmitter across nerve endings to another nerve cell, muscle cell or gland cell. It is a part of the sympathetic nervous system. It resembles for an emergency response system to danger as the acute stress response. In addition, it plays a role in regulating the level of glucose metabolism, and the immune system, increasing the heart rate and contractions force, in the "fight-or-flight" response by boosting blood flow to muscles and cardiac output via acting on the SA node [31], increasing blood flow to brain tissue and muscles, relaxing the smooth muscles of the respiratory system [32, 33], and helping to maintain or increase blood pressure depending on stress, focus, panic and excitement. Abnormal levels lead to anxiety, high blood pressure, sleep disturbances, lowered immunity [34], and pupil dilatation response [35].

Toxoplasma gondii can make an infected mouse more aggressive and less afraid of cats (definitive host) [36]. In humans toxoplasmosis may be led to schizophrenia and a desire to commit crimes [37]. Although the parasite's acute infection is asymptomatic, the chronic stage of infection causes behavioral changes [38]. The type and degree of the illness may be linked to the location and severity of the brain damage, as well as the host's and parasite strain's genetic preparedness [37]. Parasites always attack the central nervous system, either by attacking neurons directly [39] or by stimulating the immune system to produce unique chemicals that alter behavior. In any event, immunological manipulation, modification of neurotransmitters, or changes in the amounts of some essential hormones are all options for altering behavior [36]. This parasite alters the brain's neurotransmitters to bring about this behavioral shift [40]. According to studies, the toxoplasmosis infected neurons caused to produce high levels of dopamine [41, 42].

MATERIALS AND METHODS

A total of one hundred and seventy-four blood samples were collected from the visitors of Al-Sadder Teaching Hospital and the Main Blood Bank, Amarah city, Maysan province, Iraq, including 21 females and 153 males, from the period of January 2021 to May 2021. Five millilitres of venous blood were collected from each participant in gel tubes, and the serum was separated by leaving the tubes to stand for 20 minutes at room temperature to clot, then centrifuged at 3000 rpm for 10 minutes. Then the sera were placed in the Eppendorf tubes and kept at -20°C until the ELISA was performed.

The levels of IgG, IgM, dopamine and adrenaline in the sera of the participants in this study are estimated by using the ELISA test. According to the protocol attached with specific kits, each IgG or IgM was estimated individually by using anti-*Toxoplasma gondii*, IgG or IgM test kits (Demeditec, Germany). And according to the protocol attached with specific kits, each Dopamine (DA) or adrenaline (AD) level was calculated individually using ELISA-DA or ELISA-AD (Shanghai-Yehua Biological Technology, China).

Statistical analysis

The data are statistically analyzed by using $SPSS_{2020}$. Using ANOVA table, F-test, t-test. And the regression

line equation to be used to calculate the value of the studied factors.

RESULTS

The result of sera examination by ELISA (Table 1) shows that the overall *Toxoplasma gondii* seroprevalence is 52.30% (91/174). Table 1, also shows that IgM alone is detected in 17.24% (30/174) of participant's sera, IgG alone was detected in 20.12% (35/174), and IgM + IgG together was recorded in 14.94% (26/174).

Table 1. Distribution of IgM and IgG among Toxoplasma seropositive cases.

No. Exam	Immunoglobulin	No. +ve sera (%)
174	IgM alone	30(17.24)
	IgG alone	35(20.12)
	IgM+ IgG	26 (14.94)
Total +ve sera		91(52.30)

The present study (Table 2) finds that the mean dopamine level in toxoplasmosis seropositive individuals is 2.9543 $x10^{-2}$ mg ml^{-1} and in seronegative is 1.8086 $x10^{-2}$ mg ml^{-1}. It shows the level of dopamine in toxoplasmosis-infected individuals is higher about 163.347% (29.543/ 18.086) than those of uninfected individuals. There are significant differences in the level of dopamine between toxoplasmosis seropositive and seronegative individuals (F= 5.942, p=0.017). On the other hand, it showed that the level of dopamine was not affected significantly by the interaction of the human gender and toxoplasmosis (F=2.260, p= 0. 137).

This result shows (Table 3) the mean of the adrenaline level in toxoplasmosis-seropositive individuals is 2.8752$x10^{-2}$ mg ml^{-1}, while in seronegative is 1.365 $x10^{-2}$ mg ml^{-1}.

There is a significant association between the level of adrenaline and infection with toxoplasmosis (F=4.054, $p<0.05$), But it showed, the level of adrenaline was not affected significantly by the interaction between human gender-toxoplasmosis (F=0.003, p= 0.956).

Table 2. The relation between dopamine level (DA) and toxoplasmosis.

Gender	Result of immunoassay (RI)	No. Exam	DA Mean $x10^{-2}$ mg ml^{-1}
Male	Infected	7	2.3920
	non-infected	47	1.8998
	Total	54	1.9636
Female	Infected	10	3.3479
	non-infected	8	1.2725
	Total	18	2.4255
Total(1)	Infected	17	2.9543
	non-infected	55	1.8086
	Total	72	2.0791

With respect to gender; (1) DA x IR (F= 5.942, p=0.017), (RI * gender) on DA (F=2.260, p= 0. 137).

Table 3. The relation between toxoplasmosis and adrenaline (AD) level with respect to gender.

Gender	Result of immunoassay(RI)	No. exam	AD Mean $x10^{-2}$ mg ml^{-1}
Male	Infected	11	2.8114
	Non-infected	53	1.3649
	Total	64	1.6135
Female	Infected	14	2.9253
	Non-infected	8	1.3809
	Total	22	2.3637
Total(1)	Infected	25	2.8752
	Non-infected	61	1.3670
	Total	86	1.8054

(1)AD x RI, t=2.060, p=0.044, (RI * gender) on AD, F=0.003, p= 0.956).

DISCUSSION

The total seroprevalence of *T. gondii* in this study is 52.3% (91/174). This seroprevalence falls within the global infection rate which ranged from less than 10 to more than 90% [43], and in line with finding in Croatia, 47.8% to 53.8% [44]. Nonetheless, this prevalence is less than what was recorded in some Eastern Mediterranean: Kuwait, 95.5% [11], Egypt, 59.6% [45], Iran, 83.1% [46], and Bahrain, 71.5%, and in Africa: Algeria, and Namibia, were 67.5% and 74.3% respectively [14].

And it is higher than what was found in some countries of the world such as Serbia 31% (47), and 20.5% [48], Canada, 0.2% and South Korea, 2.1% [14]. While it was higher than what was recorded in some provinces of Iraq such as in Basra, 41.1% [49] and 12.4% [50], Qadisiyah, 38.7% [51], Wasit, 17.80% [52], Dohuk, 22.98% [53], and in Maysan 20% [16]. This variation in seroprevalence may be returned to vary in the diagnosis test, environmental conditions and socio-demographic factors [54], such as a person's health, age, nutrition habits, consumption of raw or undercooked meat, fruits and vegetables, hygiene practices, home ownership of cats, contact with cats, type of occupation, characteristics of the immediate environment, and geographical and climatic conditions [16, 48, 55, 56], and showed that the hot-wet regions have a great oocyst sporulation rate [57].

In this study was noted (Table 1) that the IgM alone is detected in 17.24%, of all study-population, IgG in 20.12% and IgM +IgG together in 14.94%. This result is higher than recorded in Thi Qar governorate, where were 2.7% for IgM and 35.3% for IgG [58], in Diyala 4% for IgM, 38% IgG and 2% for both IgM and IgG [59]. It can be said that cases who have IgM (17.24%) are at acute infection or maybe previous infections subjected to reactivation, and this is also confirmed by the high percentage of cases (14.94%) who have both immunoglobulins (IgM + IgG) together.

The present study (Table 2) finds that the mean of dopamine level in toxoplasmosis seropositive individuals is 2.9543 $x10^{-2}$ mg ml^{-1} and in seronegative is 1.8086 $x10^{-2}$ mg ml^{-1}. The increase in the percentage of dopamine (163.347%) is higher than what was mentioned in some previous studies in mice, where the percentage of dopamine increased to about 114% in those infected with toxoplasmosis [42]. This increase in the level of dopamine in toxoplasmosis-infected cases had been also shown in more than one study [60 – 65]. Dopamine performs many large functions in the brain [66]. Dopamine is formed in DA-ergic nerve cells from L-tyrosine with help of two enzymes, tyrosine hydroxylase and aromatic L-amino acid decarboxylase. The effect of *T. gondii* on dopamine levels may be coming by its promoting the synthesis of a neurotransmitter in the brain, it may be happing by altering the transmission of neurotransmitter signals through overexpressing an important gene due to its ability to synthesize the signaling molecule L-DOPA (3,4-dihydroxy-L-phenylalanine) [67], which is considered the root of dopamine [68], which leads to neurodegenerative diseases, and this explains by use of dopamine antagonists in psychiatric patients with toxoplasmosis reduces behavioral changes in patients [42].

The present study (Table 3) also showed a significant (p<0.05) increase in the level of adrenaline (2.8752 $x10^{-2}$ mg ml^{-1}) in toxoplasmosis-seropositive compared with negative (1.367 $x10^{-2}$ mg ml^{-1}). This increase is also mentioned in the study of Al-Hadad and his colleagues in the Al-Najaf governorate [62]. The levels of adrenaline in seropositive cases are higher about 210.329% (13.670/ 28.752) than that in negative. The increase in the levels of adrenaline may be due to the effect of toxoplasmosis on neurons in the brain or on the cells of the adrenal glands [62, 69], which are responsible for secreting adrenaline in the human body [70]. Or may be come from converting dopamine to Norepinephrine and then to adrenaline [68].

In another hand, it was shown that the level of dopamine and adrenaline in the serum of toxoplasmosis-infected males or females are higher than that of uninfected (Tables 2 and 3), but there is no statistically significant effect of the interaction between toxoplasmosis and gender on the dopamine ($F=2.260$, $p>0.05$) or adrenaline level ($F=0.003$, $p>0.05$).

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Conflict of interests

There's no conflict of interest.

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