

The Relationship between Some Chronic Diseases and Latent Toxoplasmosis in the Population of Babylon, Iraq

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Abstract

Background: *Toxoplasma gondii* is a parasite that baffled scientists for many decades with its strange behavior. It appears to have low pathogenicity, but in fact, it is different. So many studies have proven that it has severe effects on many behavioral, psychological, and physiological levels and exploits the low immunity of those who suffer from chronic diseases to prove its fierceness. **Objective:** The purpose of the current study is to look into the connection between chronic illnesses that are common in Iraqi society and latent toxoplasmosis. **Materials and Methods:** 60 healthy individuals and 180 individuals with three common chronic diseases (type 2 diabetes mellitus, chronic kidney disease [CKD], and hypertension) participated in a nested case-control study to test for anti-*T. gondii* IgG antibodies (ELISA). A formalized questionnaire was used to collect participant demographic data and acquired toxoplasma risk factors during sampling. **Results:** Anti-*T. gondii* IgG immunoglobulin was found in 13 (21.6%) control and 78 (48.2%) cases ($P = 0.002$). The results of the IgG antibody revealed that diabetics had the highest number of positive cases (48.2%), followed by patients with CKD (45.5%), and finally hypertensive patients (38.8%). However, statistical analysis revealed no statistically significant differences between the number of positive toxoplasmosis cases and the type of sample examined (P value = 0.51). Other demographic factors had no discernible impact on infection rates. **Conclusion:** We conclude that there is a close connection between chronic *Toxoplasma* infection and some common chronic illnesses, which are thought to be risk factors for the spread of parasitic infection.

Keywords: Chronic kidney disease, diabetes mellitus, hypertension, latent toxoplasmosis

INTRODUCTION

Toxoplasma gondii is an unusual parasite, in that it has no specificity and attacks a wide variety of hosts, causing a great deal of damage as well as infection with it being associated with a high mortality rate in the general population.^[1] *Toxoplasma gondii* infects more than a third of the global population.^[2] The final hosts of *T. gondii* are members of the Felidae family, which comprises both wild and domestic cats, whereas all other animals act as intermediate hosts.^[3,4] Several studies have dealt with the relationship of this parasite in many diseases.^[5-7] These studies indicated two important things, namely that the parasite may be the cause of the occurrence of that disease or that this disease may lead to weak immunity and thus increase susceptibility to infection with the parasite.

Diabetes mellitus (DM) is a common disease that spread in all countries of the world, including Iraq. It is marked

by hyperglycemia induced by a lack of insulin secretion (type 1 diabetes) or a failure to react adequately to insulin in recipient cells (type 2 diabetes), and it is thought that genetic causes, autoimmune mechanisms, and environmental factors are all involved.^[8] This disease has severe consequences in the body, followed by immune changes that make the person infected with it vulnerable to many other diseases. Many studies have exposed diabetics to infection with some pathogens such as bacteria, viruses, and parasites. Catchpole *et al.*^[9] conducted a systematic review and meta-analysis of previous studies, supporting

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that *T. gondii* infection may be associated with type 1 diabetes. In addition, *T. gondii* seroprevalence was reported to be high in two forms of DM (1 and 2) individuals compared to healthy individuals in southwest Iran.^[10] Although previous studies found a link between chronic *T. gondii* infection and DM, there are still many unknowns about *T. gondii* role in the pathogenesis of DM.

Chronic kidney disease (CKD) is very common and expensive to treat, the synthesis of several hormones by the kidneys affects immunity, either directly or indirectly. They include vitamin D, which regulates the equilibrium in the bone environment and regulates the activity of macrophages.^[11] At the turn of the current millennium, parasites were already high on the list of potentially possible factors cause kidney disease.^[12] Twenty parasites are linked to kidney disease out of the 342 parasites that affect humans.^[13]

Another common chronic disease associated with age is high blood pressure (hypertension), which has a direct role in atherosclerosis.^[14] The immune system and hypertension are closely related because high blood pressure is also accompanied by immune-inflammatory cell infiltration, particularly macrophages, and increased cytokine production results in structural and muscular changes in blood vessels which cause rising blood pressure.^[15] Many factors affect and have a relationship with high blood pressure, including age, gender, body mass, and diabetes.^[16] Previous studies have linked the latter disease to many pathogens,^[17-19] while other studies have failed to establish a relationship between infectious agents and cardiovascular diseases, including blood pressure.^[20,21]

As far as we know, there are no substantial findings linking toxoplasmosis to the chronic diseases listed above, except for MD, there is no knowledge about the relationship between toxoplasmosis and these diseases in Iraq. It is important to note that there's some evidence linking these diseases with *Toxoplasma* infection in Iraq. As a result, the latest research was carried out to determine the seroprevalence of *T. gondii* infection in patients with three common local diseases in Babylon province.

MATERIALS AND METHODS

Sample gathering technique

All participants ($N = 240$) in this nested case-control study were adult men and women from Babylon, Iraq, specifically from Imam Al-Sadiq Hospital (Turkish Hospital) and some private medical laboratories for the period from July to September of 2022. 60, of whom were healthy and 180 of whom had one from three common chronic diseases in Iraq (56 DM type 2, 44 CKD and 80 hypertension).

The diagnosis of the disease relied upon a specialist physician who conducted medical examinations for them,

pointing out that some patients suffer from the disease for a long time and are undergoing treatment, some patients with kidney failure are subjected to dialysis. Each subject was provided a sample of venous blood (about 5 mL), and the sera were isolated. A specially created questionnaire was used during the sampling to gather data on the participants' demographics and their exposure to *Toxoplasma* risk factors. Demographic data including age, gender, residence, and smoking status were collected from all participants. Samples were moved using the cold box to the laboratory at the University of Babylon, College of Science for Women, where they were kept at -20°C until testing.

Toxoplasma gondii IgG antibody detection by ELISA

The Enzyme Linked Immunosorbent Assay method was used to test sera samples with a TOXO IgG kit (ACON ELISA kit, China), by the instructions provided by the manufacturer.

Statistical analysis

MedCalc is a statistical software package for biomedical research by Ostend, Belgium. Statistics include more than 220 statistical tests, procedures and graphs. ROC curve analysis, method comparison and quality control tools for Windows program was used to analyze the data. The Chi-square test was used to compare the independent variables' frequency distributions between groups. It was deemed statistically significant if P value was 0.05 or less.

Ethical approval

The study was carried out in conformity with the ethical standards set forth in the Helsinki Declaration. Before a sample was taken, it was done with the patient's verbal and analytical consent. According to the paper dated July 8, 2022, a local ethics committee evaluated and approved the study protocol, subject information, and consent form to obtain this approval.

RESULTS

Table 1 shows the socio-demographic results of the patients and the control group. It revealed that the highest rates of chronic disease cases were in the two age groups 41–50 and >50 , as the percentage was equal, which is 31.7%. The percentage of male patients included in the study constituted 53.9% of the patients, whereas the remaining percentage comprised female patients, compared to 55% and 45% for men and women, respectively, in the control group. In terms of patient and control group distribution in rural and urban areas, 62.2% of the patient population lived in urban areas compared to 56.7% of the control group, whereas 37.8% lived in rural areas compared to 43.3% of the control group. The percentage of current smokers was 28.9% in the patient's group, compared to 26.7% in the control group.

Table 1: Demographic and social characteristics of the people in the study based on the type of chronic disease

Variables	Ranking	Patients (n = 180)								Control (n = 60)	
		Diabetes 56		chronic kidney disease 44		Hypertension 80		Total 180		n	%
		n	%	n	%	n	%	n	%		
Age/year	21-30	6	10.7	13	29.5	12	15.0	31	17.2	12	20.0
	31-40	10	17.9	10	22.7	15	18.8	35	19.4	16	26.7
	41-50	18	32.1	9	20.5	30	37.5	57	31.7	12	20.0
	>50	22	39.3	12	27.3	23	28.8	57	31.7	20	33.3
Gender	Male	30	53.6	20	45.5	47	58.8	97	53.9	33	55
	Female	26	46.4	24	54.5	33	41.3	83	46.1	27	45
Residence	Rural	29	51.8	22	50	17	21.3	68	37.8	26	43.3
	Urban	27	48.2	22	50	63	78.8	112	62.2	34	56.7
Smoking	Never	28	50.0	19	43.2	36	45.0	83	46.1	39	65.0
	Past smoker	10	17.9	15	34.1	20	25.0	45	25.0	5	8.3
	Current smoker	18	32.1	10	22.7	24	30.0	52	28.9	16	26.7

*(mean significant $P < 0.05$)**Table 2: The percentage of IgG antibodies for *T. gondii* in the control and patients groups**

Groups	Negative		Positive	
	n	%	n	%
Patients (n = 180)	102	51.8	78	48.2
Control (n = 60)	47	78	13	21.6
Total (n = 240)	149	62.1	91	7.9
The calculated value of χ^2	8.97	df 1	$P = 0.002^*$	

*(mean significant $P < 0.05$)**Table 3: The percentage of IgG antibodies for *T. gondii*, depending on the type of chronic disease**

IgG antibodies	Patients (n = 180)					
	Diabetes 56		Chronic kidney disease 44		Hypertension 80	
	n	%	n	%	n	%
Negative	29	51.8	24	54.5	49	61.3
Positive	27	48.2	20	45.5	31	38.8
The calculated value of χ^2	1.31	df 2	$P = 0.51$			

*(mean significant $P < 0.05$)

Table 2 shows the prevalence of gamma globulin antibodies to *Toxoplasma* in both patients and control groups; anti-*T. gondii* IgG antibodies were present in 78 (48.2%) of the cases and 13 (21.6%) of the controls. The patient's group had a higher seroprevalence of *T. gondii* rate than the control as supported by statistical analysis.

The findings of the IgG antibody by ELISA test are shown in Table 3. It was found that diabetics had the largest number of positive cases (48.2%), followed by individuals with CKD (45.5%), and eventually patients with elevated blood pressure (38.8%). However, the statistical analysis did not show significant differences between the number of positive cases of toxoplasmosis and the type of sample examined.

The percentage of chronic infection with *Toxoplasma* in diabetic patients was the highest (80.0%) in the age group 31–40 years, where the patients with renal failure and high blood pressure 41–50 and 21–30 years were the highest infection respectively. The control group also recorded the highest infection (33.3%) in the age group 41–50 years. In any case, there was no statistical difference except in hypertensive patients [Table 4].

The chi-square analysis showed that there were no significant differences in toxoplasmosis between male and female patients in all groups except patients with high blood pressure, as there was a significant increase in the infection rate in women (51.5%) compared to men (29.8%) [Table 5].

Table 4: Effect of age group on the percentage of IgG antibodies for *T. gondii* in groups of patients and control

Age/year	Patients (n = 180)						Control (n = 60)	
	Diabetes		Chronic kidney disease		Hypertension		+Ve	%
	+Ve	%	+Ve	%	+Ve	%		
21–30	3	50.0	7	53.8	9	75.0	2	16.7
31–40	8	80.0	3	30.0	8	53.3	2	12.5
41–50	6	33.3	7	77.8	9	30.0	4	33.3
>50	10	45.5	3	25.0	5	21.7	5	25.0
Total	27	48.2	20	45.5	31	38.8	13	21.7
The calculated value of χ^2	5.718		7.151		11.760		2.062	
P value	0.127		0.067		0.008*		0.560	

*(mean significant $P < 0.05$)**Table 5: Effect of gender on the percentage of IgG antibodies for *T. gondii* in groups of patients and control**

Gender	Patients (n = 180)						Control (n = 60)	
	Diabetes		Chronic kidney disease		Hypertension		+Ve	%
	+Ve	%	+Ve	%	+Ve	%		
Male	16	53.3	12	60.0	14	29.8	7	21.2
Female	11	42.3	8	33.3	17	51.5	6	22.2
Total	27	48.2	20	45.5	31	38.8	13	21.7
The calculated value of χ^2	0.678		3.129		3.856		0.009	
P value	0.410		0.077		0.0496*		0.925	

*(mean significant $P < 0.05$)**Table 6: Effect of residence on the percentage of IgG antibodies for *T. gondii* in groups of patients and control**

Residence	Patients (n = 180)						Control (n = 60)	
	Diabetes		Chronic kidney disease		Hypertension		+Ve	%
	+Ve	%	+Ve	%	+Ve	%		
Rural	9	31.0	10	45.5	11	64.7	6	23.1
Urban	18	66.6	10	45.5	20	31.7	7	20.6
Total	27	48.2	20	45.5	31	38.8	13	21.7
The calculated value of χ^2	7.110		0		6.128		0.054	
P value	0.008*		1		0.013*		0.817	

*(mean significant $P < 0.05$)**Table 7: Effect of smoking on the percentage of IgG antibodies for *T. gondii* in groups of patients and control**

Smoking	Patients (n = 180)						Control (n = 60)	
	Diabetes		Chronic kidney disease		Hypertension		+Ve	%
	+Ve	%	+Ve	%	+Ve	%		
Never	9	32.1	8	42.1	9	25	7	17.9
Past smoker	8	80	6	40	10	50	2	40
Current smoker	10	55.6	6	60	12	50	4	25
Total	27	48.2	20	45.5	31	38.8	13	21.7
The calculated value of χ^2	7.332		1.119		5.214		1.413	
P value	0.026*		0.571		0.074		0.494	

*(mean significant $P < 0.05$)

The seroprevalence of IgG anti-toxoplasma antibodies in patients between the countryside and the city varies according to the type of chronic disease. It was found that the highest seroprevalence rate in the city was in patients with diabetes, whereas the ratios were equal for kidney patients between the countryside and the city, offset by a higher ratio in the countryside for hypertensive patients, and no significant difference was recorded in the control group [Table 6].

Except for diabetics, there were no significant differences according to the chi-square analysis, in chronic parasite infection among smoking cases in all groups. However, in diabetics there was a significant increase in infection rates among former smokers (80%) compared to current smokers (55.6%), and among non-smokers (32.1%) [Table 7].

DISCUSSION

The current results indicate that the seroprevalence of IgG antibody, which is indicative of chronic infection with *T. gondii*, was higher in patient groups (DM, chronic renal impairment, and hypertension) than in control groups (healthy subjects). The reason may be due to the low level of immunity in these patients and thus being exposed to many pathogens, including this parasite. Because of patients' poor response to medications prescribed for chronic conditions such as diabetes and high blood pressure in underdeveloped nations such as Iraq, patients with diabetes-related hypertension, therefore, have higher death rates, higher hospital admissions, and less favorable health outcomes.^[22] There are previous studies that showed a high incidence of *Toxoplasma* parasite in people with various diseases. Naval *et al.*^[6] reported that anti-*T. gondii* IgG and IgM antibodies were found to be more common in patients with chronic liver disease than in the control group.

The higher of parasitic infection proportion in chronic disease patients compared to the control group may be explained by decreased cellular and humoral immune responses in chronic disease patients leading to the reactivation of infections that have been dormant for a long time.^[23,24]

The results of the examination using the IgG antibody ELISA test showed the highest percentage of positive cases in diabetics, followed by people with kidney failure, then finally the patients with high pressure. Overall, the latest theory assumes that toxoplasmosis raises the risk of developing diabetes, whereas diabetic patients are more susceptible to opportunistic infections including toxoplasmosis.^[25-28] Research conducted by Beshay *et al.*^[29] indicated that an increase in serum glucose concentration was associated with an increased prevalence of apoptotic signs in the islets of Langerhans and a concomitant decline in insulin production that occurs during *Toxoplasma*

infection. According to a meta-analysis study by Majidiani *et al.*^[30] chronic toxoplasmosis may be a risk factor for type 2 diabetes. *Toxoplasma gondii* and type-1 diabetes are positively associated, according to the research paper published in 2021.^[31]

Toxoplasma gondii infection is linked to blood pressure through the parasite's manipulation of hormones and neurotransmitters.^[32,33] It can significantly raise dopamine levels in the body by using dopaminergic nerve cells as dopamine-producing neurons,^[34,35] and also dopamine is well known to raise blood pressure.^[36] CKD may be caused by some immune disorders. Kidney failure can also damage the immune system, and it induces protein to be excreted by the body as kidney failure progresses, because protein is very important to the immune system. Protein secretion is critical because proteins make up certain immune system components including enzymes and antibodies.^[37] Patients with CKD are frequently immunosuppressed and prone to various infections. Immune system changes make patients more susceptible to infection, which raises the risk and exacerbates inflammation and cardiovascular diseases.^[38]

Chronic infections with *Toxoplasma* did not pose significant differences depending on the age stages of diabetic patients, kidney patients, and the healthy group, but it was significantly high in the young group (21–30 years) among hypertensive patients. The effects of some diseases may interfere with age on the rate of infection with the parasite, as age constitutes a risk factor for chronic diseases, and thus helps exposure to opportunistic pathogens. Our current study does not agree with other studies, as most of them confirmed an increase in *Toxoplasma* infection with increasing age, including the study of Mihu *et al.*,^[39] which indicated an increase in the rates of infection with this parasite in the older age groups of women in Romania. The difference in the results may be because the current study did not take all the information from the participants regarding other risk factors, such as eating meat or raising cats at home, the economic situation, or the educational level. These factors may have contributed to the percentage of seroprevalence of *T. gondii* among different age groups.

The results of parasitic infection by *T. gondii* in all study groups indicate that there are no significant differences between male and female patients, except that there is a slightly significant difference in patients with high blood pressure, as the infection rate was higher in women than men. It is consistent with the findings of Khabisi *et al.*^[40] in Iran, who found no significant association between *T. gondii* seropositivity and sex.

When studying the effect of the population area, the results varied about the infection rate between the rural and the urban in the groups under study. The statistical analysis did not record significant differences in the group

of patients with kidney failure and the control group, a significant increase was recorded in the infection rate in the urban in the group of diabetic patients. On the contrary, the infection rate has recorded an increase in patients with high blood pressure in the rural. The high rates of infection in urban residents (diabetic patients) may be due to an increase in the number of cats in cities, as it is more common for cats to spread in Iraqi homes in cities than in the countryside. While the increase in infection among the rural population (hypertensive patients) can be explained by the exposure of individuals in rural areas to contaminated water and soil.^[41] As the handling of animals is a factor that may contribute to the rise prevalence of infection among farmers living in rural areas.^[42]

The significant difference in the percentage of *Toxoplasma* infection depending on the smoking status was achieved only in the group of people with diabetes, as the highest percentage (80%) was among people who had smoked in the past. According to a study by Alvarado-Esquivel *et al.*,^[43] *T. gondii* seropositivity in Mexican blood donors was linked to tobacco use (odds ratio = 2.09, $P = 0.04$). Although the relationship between tobacco use and infection with the parasite is not understood, they attributed this to several possible causes, including cigarette use contributes to the transmission of parasitic infection through the mouth as a result of not washing hands when smoking. As well as the common relationship of tobacco and *Toxoplasma* in increasing the secretion of dopamine in the brain. In contrast, the findings of the study by Bahreini *et al.*^[44] indicate that *Toxoplasma* infection can lessen the craving for tobacco because the seroprevalence rate of *Toxoplasma* infection is higher in non-smokers than in smokers.

CONCLUSIONS

We conclude from the current study that there is a close relationship between chronic *Toxoplasma* infection and some chronic diseases, which are considered risk factors for the spread of parasitic infection. Patients with diabetes have the highest rate of infection with the parasite. Other factors did not have a clear effect on the incidence rate.

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Conflicts of interest

There are no conflicts of interest.

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