The Study of Association Between *Toxoplasma gondii* Infection with Ischemic Heart Diseases

Tariq.Q.Tallab* , Jabbar R. Al-Autabbi *,Dhiaa.k.Al-Umer**

ABSTRACT:

BACKGROUND:

Coronary artery disease (CAD) is the main cause of mortality in industrial and developing countries. New risk factors including infections are under investigation as potential factors. One of these infectious agents is *Toxoplasma gondii,* few data have been published on the association of atherosclerosis (the usual cause of ischemic heart disease) and *Toxoplasma gondii* infection. The **OBJECTIVE:**

Was to investigate potential role of *T.gondii* infection as a risk factor for coronary atherosclerosis in ischemic heart disease patients and the correlation between *T.gondii* with other cardiovascular risk factors

PATIENTS AND METHODS:

This study was conducted on (58) patients with Ischemic Heart Diseases attended cardiac care unite in Al-Hussein teaching hospital in Nasseriya city, southern Iraq and 32 healthy controls ,all are free from clinically evident disease were attending the blood bank in Nasseriya city between November 2010 to the end of August 2011. the sera of the patients and control groups were tested for *T.gondii* antibodies using Enzyme-Linked Immunosorbent Assay (ELISA) technique. The obtained data was analyzed and the results were tabulated.

RESULTS:

22(37.9 %) in the case group and 11(34.4 %) in the control group were seropositive for *T.gondii* antibodies, odds ratio (OR) 1.167 . P= 0.915 . And there were no association between risk factors and *Toxoplasma gondii* infection, (Table 2, 5). (Figure 1).

CONCLUSION:

This study shows that there is no association between *Toxoplasma gondii* infection and ischemic heart disease

KEYWORDS: toxoplasma gondii, coronary artery disease, atherosclerosis

INTRODUCTION:

Coronary artery diseases (CAD) are the main causes of death in developed countries. Atherosclerosis is considered as the pathology of these diseases [(1)]. The reasons of the risk of coronary atherosclerosis are not the same in all patients; different causes may result in the occurrence and the progression of atherosclerosis in different patients. In humans, no single factor can account for all the causes of CAD, in high percentage of patients have none of traditional risk factors such as hypertension, smoking, obesity, hypercholesterolemia or genetic predisposition [(1)]. Due to this fact, medical researchers are beginning to find other risk factors to express causes of coronary atherosclerosis incidence. Clinical and experimental studies indicate that inflammatory diseases have a role in atherosclerosis [(2)]. Many epidemiological investigations have shown significant relationship between coronary ischemia and various infectious agents such as bacterial and viral [(3,4,5)]. now Atherosclerosis considered as a chronic inflammatory disease, and systemic infections are thought to play an important role in initiating and/or perpetuating the pathophysiology of atherosclerotic lesions. In fact, some studies indicate that bacterial and viral pathogens could be responsible for atherosclerotic development [(6)] *Toxoplasma gondii* is an obligate intracellular protozoan parasite which is spread worldwide, infecting as many as one billion people. In the acute phase of infection, *T. gondii* tachyzoites trigger the synthesis of IL-12 and other costimulatory cytokines, which initiate the synthesis of IFN-y by NK cells and $CD4^+$ $CD8^+$ T lymphocytes [(7,8,9,10)]. In the chronic phase, levels of

* Baghdad Medical College.
** Thi- Qar Medical College.

proinflammatory cytokines decrease, but highly polarized Th1 $CD4^+$ T lymphocytes as well as $CD8^+$ T lymphocytes are thought to maintain a robust IFN-y production, a main component of the host resistance to infection with *T. gondii* [11,12].

Toxoplasma gondii, in turn, is dependent on host cholesterol for optimal intracellular growth and replication. As a result, host cholesterol will be cleared from the blood, reducing plasma low-density lipoprotein, a crucial atherosclerosis risk factor. On the other hand, *T. gondii* infection elicits an important Th1 systemic inflammatory response in the host. Therefore, this additional proinflammatory stimulus may impose an enhanced pro-atherogenic environment in the host. As result, the association between these two diseases in one individual could change the course of atherosclerosis [13].

PATIENTS AND CONTROLS:

this study was conducted on (58) Ischemic Heart Diseases patients (their age ranging between 40 - 80 years old with mean age (62.2±7.71) attending cardiac care unite in Al-Hussein teaching hospital in Nasseriya city, southern Iraq and 32 healthy control, all are free from clinically evident disease were attending the blood bank in Nasseriya city between November 2010 to the end of August 2011.

METHODS:

Firstly questionnaire was filled followed by laboratory investigation, the sera of the patients and control group were tested for *T.gondii* anti-IgG antibodies using Enzyme-Linked Immunosorbent Assay (biocheck, Inc. Foster city, USA). Results were expressed as the optical density. Alevel > 32 IU/ml was considered positive. Statistical analysis was done using SPSS version 16 computer software (Statistical package for Social Sciences).The mean value with the standard deviation (SD) for each value was determined. P-value less than 0.05 was considered indicative of statistically significant difference.

RESULTS:

The mean age of patients was 62±7.7, and in controls, 43 ± 8.6 years. Comparison of these values by an independent sample test showed no statistical difference (*P*=0.460). The sex ratio in cases was 70.7% men and 29.3% women, and in controls, 96.9% men and 3.1% women. Comparison of these ratios by Chi-square test showed statistical difference (*P*< 0.05) (Table 1) in patient group, 37.9% of patients were seropositive for *T.gondii* anti-IgG antibodies, while in controls, 34.4% showed positive anti-IgG antibodies for *T.gondii*. Comparison of these ratios by Chi-square test showed no statistical difference (*P*>0.05) (Table 2). Results of assessing risk factors showed a significant relationship between IHD and each risk factor (Table 2). The mean age of seropositive patients was 61±8.9 yr and in seronegative patients was 63.06 ± 6.8 yr. A comparison of these averages showed no statistical difference, (Table 3). In the seropositive patients, the sex distribution was as follows: 72.2% men and 27.3% women. In contrast with seronegative patients, in seronegative ones, the sex distribution was 69.4% men and 30.6% women which in chi-square comparison did not show any statistical difference (*P*>0.05) (Table 3). There was no significant association between *T.gondii* and traditional risk factors, (Table 4).

Table 1: Distribution of study groups according to the age and gender

characteristics	Patients NO. (%)	Controls NO.(%)	P-value
Age mean(years)	62 ± 7.7	43 ± 8.6	0.460
Male	41 (70.7)	31 (96.9)	0.007
Female	17 (29.3)	1 (3.1)	

Table 2: Main clinical features and seropositivity for *T.gondii* of patients and control groups

characteristics	Seronegative *T.gondii* NO.(%)	Seropositive *T.gondii* NO.(%)	P-value
Age mean(years)	63.06 ± 6.8	60.77 ± 8.9	0.278
Male	25 (69.4)	16 (72.7)	1.000
Female	11 (30.6)	6 (27.3)	

Table 3: Distribution of patients with and without *T.gondii* infection according to age and gender.

Clinical data	Seronegative *T.gondii* NO.(%)	Seropositive *T.gondii* NO.(%)	P-value
Hypertension	28 (77.8)	20 (90.9)	0.354
Diabetes	14 (38.9)	9 (40.9)	1.000
Hyperlipidemia	10 (27.8)	9 (40.9)	0.456
Smoking	19 (52.8)	14 (63.6)	0.591
Family History	5 (13.9)	6 (27.3)	0.359

Table 4: Main clinical features of patients with and without *T.gondii* infection.

Clinical data	Patients NO (%)	Controls NO(%)	P-value
Hypertension	48 (82.8)	12 (37.5)	0.0001
Diabetes	23 (39.7)	3 (9.4)	0.005
Hyperlipidemia	19 (32.8)	2 (6.2)	0.01
Smoking	33 (56.9)	20 (62.5)	0.769
Family History	11 (19.0)	6 (18,8)	1.00
Seropositive *T.gondii*	22 (37.9)	11 (34.4)	0.915

DISCUSSION:

Atherosclerotic lesions are characterized by progressive accumulation of lipids, macrophages, natural killer (NK) cells, T and B cells, smooth muscle cells, and fibroproliferative elements in the intima of arteries [14]. Therefore, atherosclerosis is considered a chronic inflammatory disease *Toxoplasma gondii* is an intracellular protozoan parasite which is found worldwide. *T. gondii* is unable to produce cholesterol via mevalonate [15]. In consequence, the cholesterol acquisition occurs by lipoprotein endocytosis, using low-density lipoprotein receptor (LDLr), it is not clear if *T. gondii* infection would increase atherosclerosis by enhancing systemic inflammation or reduce atherogenesis as a consequence of increased clearance of circulating LDL[16]. According to our knowledge this is the first study in Iraq, Our study shows the significant association between known risk factors of coronary disease such as diabetes, hypertension and hyperlipidemia with CAD (Table1). Besides, in patients, there was no significant relation between *T. gondii* infection and diabetes, hypertension and hyperlipidemia (Table 2). The Logistic regression analysis showed no relationship between *T. gondii* and CAD (P>0.05), therefore *T. gondii* infection can not introduced as a risk factor of CAD incidence. There are very few published research on this topic. Lobzin IuV,et al 2005 in case-control study included 64 patients with (CAD) and 38 healthy controls. Shows diagnostically significant elevation of the serum levels of IgG antibodies to *chlamydia pneumonia, ,Herpes simplex virus 1,2 and T.gondii* was associated with development of atherosclerosis and CAD [17].In addition, in case-control study on ApoE-Deficient Mice, Portugal,et al,2004 discovered that infection with Toxoplasma gondii increases atherosclerotic lesion in these Mice[18].

Table 5: Distribution of study groups according to *Toxopalasma gondii* IgG.

Study Groups	*T.gondii* IgG		Total	OR	95% C.I.	P -value
	Yes	No				
IHD	22 (37.9%)	36 (62.1%)	58 (100.0%)	1.167	0.47- 2.875	0.915
Control	11 (34.4%)	21 (65.6%)	32 (100.0%)			
Total	33 (36.7%)	57 (63.3%)	90 (100.0%)			

CONCLUSION:

The link between *Toxoplasma gondii* infection and coronary atherosclerosis requires further studies. *Toxoplasma gondii* infections are a potentially curable diseases and for this reason, the identification of this condition as a coronary risk factor may have important implications for the prevention of ischemic heart disease.

Recommendations:

1. Studies with larger patients and controls samples
2. Further studies, with more sophisticated investigational methods, are needed.For example, using polymerase chain reaction (PCR) tests for detection of remnant DNA molecules of *Toxoplasma gondii*.

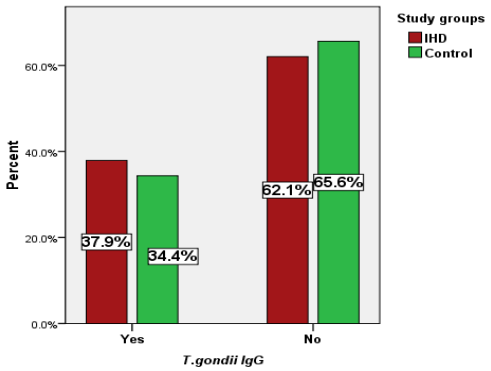

Figure 1: Distribution of study groups according to *Toxopalasma gondii* IgG

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