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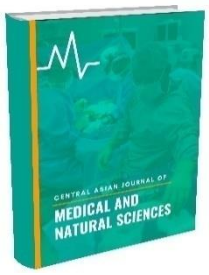

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Diagnostic Levels of Some Biochemical (RBS, Cholesterol, Triglyceride, HDL, VLDL, LDL, Urea, Creatinine and Total Protein) in Patients and Healthy Controls Subjects, Markers of Toxoplasma Infection in Patients with Acute Coronary Syndrome

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Abstract: The current study was conducted to evaluate the current situation of the cardiac involvement due to the presence of Toxoplasma gondii infection in patients in Al-Diwaniyah City, Iraq. The present study enrolled randomly 120 patients with Acute coronary syndrome and 60 healthy control to surveillance Toxoplasma infection by monitored the dynamic changes of IgG findings and correlate that with myocarditis at different levels (age, gender, blood profiles of some features, and blood groups). The present results showed 42 (35.0%) of Acute coronary syndrome have active or previous Toxoplasma infection by finding positive results of IgG.

According to the blood profile, the mean levels of random blood sugar (RBS) were 221.46 ± 57.62 mg/dL, 203.73± 58.31 mg/dL, 108.60± 14.9 mg/dL and 93.3± 7.33 mg/dL, in Acute coronary syndrome patients with toxoplasmosis. Also the Mean levels of cholesterol were 227.56 ± 35.52, 202.90± 26.05, 162.06± 17.8 and 185.6 ± 8.1, Acute coronary syndrome patients with toxoplasmosis. Also the Mean levels of Triglyceride were 196.0± 70.31, 182.3± 54.86, 127.33± 19.9 and 126.83± 17.4, Acute coronary syndrome patients with toxoplasmosis.

Key words: Toxoplasma infection, acute coronary syndrome, blood group distribution, prevalence, diagnostic markers.

The urea levels showed the mean levels of blood urea highly significant increase in Acute coronary syndrome patients with toxoplasmosis in compared to other groups, 53.73± 13.77 mg/dl versus 39.83± 9.18 mg/dl, 32.86± 8.06 mg/dl and 30.83± 6.32 mg/dl respectively, ($P < 0.001$). The Hb and Pcv % demonstrated that Hb levels were 11.56 ± 2.14, 12.09± 2.49, 13.26± 1.93 and

12.7± 2.30, in Acute coronary syndrome patients with toxoplasmosis. Also the Mean levels of Pcv % were 37.76± 6.1, 39.06± 7.09, 42.13± 5.05 and 41.06 ± 6.42, Acute coronary syndrome patients with toxoplasmosis.

The findings of the current study suggest potential correlation between myocardial involvement and the infection of toxoplasmosis in regards to different biomarker predictors.

INTRODUCTION

Toxoplasmosis is a communicable disease that commonly occurs in tropical and subtropical developing countries around the world (Ryan et al., 2019). An increased prevalence is seen in rural areas and populations with low socioeconomic status (Pappas et al., 2009b). Toxoplasmosis is caused by T. gondii, a protozoan parasite that spends most of its life cycle inside cats. It spreads easily to humans, either by consumption of undercooked meat, by contaminated water, or by contact with feline feces (Zhou et al., 2021).

T. gondii infection in healthy humans and animals becomes asymptomatic because host innate and adaptive immunity resists its initial proliferation and eradicates most of the parasites. Infection of monocytes by a T. gondii tachyzoite strongly induces innate immune responses such as the production of pro-inflammatory cytokines, resulting in the activation of adaptive immune responses mediated by T and B cells (Sasai et al., 2018).

Cardiovascular disease is the most common cause of mortality and responsible for about 30% of deaths worldwide. Coronary artery disease is known to be the deadliest cardiovascular disease accounting for more than 50% of heart deaths. As fatal toxoplasmosis has been reported in liver and bone marrow, hematopoietic stem cell transplant recipients, it has been reported as a significant human pathogen for heart transplantation. In this situation, cysts may be Toxoplasma activated after being transplanted to a host with the weakened immune system. In cardiac transplant recipients, the diagnosis of freshly synthesized IgG antibodies is valuable in case of positive donors. Studies have shown that patients with chronic cardiovascular disease are often exposed to opportunistic infections such as toxoplasmosis, due to general body weakness and immunocompromised state (Khademvatan et al., 2020).

A biomarker is an attribute that is measured and evaluated as an indicator of a pathogenic process; therefore, several biomarkers are used as indicators to cardiovascular diseases (Group et al., 2001). The increase of triglycerides (TG) or total cholesterol (TC) is associated with cardiovascular disease; moreover, the increase of low-density lipoprotein cholesterol (LDL-C) is considered a major risk for cardiovascular dysfunction (Nordestgaard and Varbo, 2014). VLDL is also known to contribute to the development of atherosclerotic cardiovascular disease. Large VLDL particles, which are subclassified according to their size by nuclear magnetic resonance spectrometry, are significantly correlated not only with atherosclerosis, but also with insulin resistance and diabetes incidence (Lee et al., 2022).

Creatinine as a marker of kidney function is considered to be a predictor for worse outcomes in ACS patients (Shiraishi et al., 2016). Additionally, urea can be a marker that reflects disorders of cardio renal function and neurohormonal activation. In patients with heart failure, high urea levels are a marker of strong mortality compared to creatinine and this relationship has also been shown in patients with ACS (Gibson et al., 2003, Chen et al., 2012). The aim of the study

This study aimed to find, evaluate and determine whether there is a correlation between acute coronary syndrome with Toxoplasmosis in a group of patients from Al-Diwaniyah city center and

Investigate the changes in some biochemical markers in patients with acute coronary syndrome, those who have anti-Toxoplasma Abs and compare that with apparently healthy controls.

Method and Material

Study Design:

This research employed a cross-sectional study design to investigate the prevalence of Toxoplasma infection in patients with acute coronary syndrome (ACS) and explore the association between Toxoplasma infection, serum IgG levels, and blood group distribution. The study aimed to collect data from both patient and control groups and analyze them to draw conclusions about the relationship between Toxoplasma infection and cardiovascular health.

Participants:

The study included two groups: ACS patients and a healthy control group. The ACS patient group consisted of individuals diagnosed with acute coronary syndrome, while the control group comprised individuals without any known cardiovascular diseases or symptoms. The sample size consisted of 120 ACS patients and 180 individuals in the control group.

Statistical Analysis:

The collected data were subjected to statistical analysis to assess the significance of the findings. Descriptive statistics were used to summarize the characteristics of the study population, including demographic information and distribution of serum IgG levels and blood group types. To evaluate the association between Toxoplasma infection and ACS, the chi-square test was employed. The test examined the differences in IgG positivity rates and blood group distributions between the ACS patient group and the control group. The significance level was set at $P \leq 0.05$ to determine statistical significance.

Results

Levels of some biochemical markers (RBS, Cholesterol, Triglyceride, HDL, VLDL, LDL, urea, creatinine and total protein) in patients and healthy controls subjects.

The comparison of some biochemical markers between patient groups and control group subjects has been carried out and the results were demonstrated in table (1). Mean levels of random blood sugar (RBS) were 221.46 ± 57.62 mg/dL, 203.73± 58.31 mg/dL, 108.60± 14.9 mg/dL and 93.3± 7.33 mg/dL, in Acute coronary syndrome patients with toxoplasmosis, Acute coronary syndrome patients without toxoplasmosis, Healthy with toxoplasmosis and Healthy without toxoplasmosis respectively; the mean levels was higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant ($P < 0.001$). Also the Mean levels of cholesterol were 227.56 ± 35.52, 202.90± 26.05, 162.06± 17.8 and 185.6 ± 8.1, Acute coronary syndrome patients with toxoplasmosis, Acute coronary syndrome patients without toxoplasmosis, Healthy with toxoplasmosis and Healthy without toxoplasmosis respectively; the mean levels was higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant ($P < 0.001$). Also the Mean levels of Triglyceride were 196.0± 70.31, 182.3± 54.86, 127.33± 19.9 and 126.83± 17.4, Acute coronary syndrome patients with toxoplasmosis, Acute coronary syndrome patients without toxoplasmosis, Healthy with toxoplasmosis and Healthy without toxoplasmosis respectively; the mean levels was higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant ($P < 0.001$).

According to blood urea levels, the present study show the mean levels of blood urea highly significant increase in Acute coronary syndrome patients with toxoplasmosis in compared to

other groups, 53.73± 13.77 mg/dl versus 39.83± 9.18 mg/dl, 32.86± 8.06 mg/dl and 30.83± 6.32 mg/dl respectively, (P < 0.001). Also the mean levels of serum creatinine highly significant increase in Acute coronary syndrome patients with toxoplasmosis in compared to other groups, 1.22± 0.36 mg/dl versus 1.11± 0.37 mg/dl, 0.82± 0.21 mg/dl and 0.93± 0.126 mg/dl respectively, (P < 0.001).

Table (1): Levels of some biochemical (RBS, Cholesterol, Triglyceride, HDL, VLDL, LDL, urea, creatinine and total protein) in Patients and healthy controls.

	Cases–control comparison				
	Patients with toxoplasmosis N=42	Patients without toxoplasmosis N=78	Healthy with toxoplasmosis N=6	Healthy without toxoplasmosis n=54	Total P value
Random blood sugar (RBS) mg/dl					
Mean± SD	221.46 ± 57.62 ^{A}	203.73± 58.31 ^{A}	108.60± 14.9 ^{B}	93.3± 7.33 ^{B}	< 0.001 † HS
Range	110.0- 325.0	121.0 – 322.0	88.0 – 136.0	84.0 – 112.0	
Different latters denote to the significant differences at p< 0.05					
Cholesterol mg/dl					
Mean± SD	227.56 ± 35.52 ^{A}	202.90± 26.05 ^{B}	162.06± 17.8 ^{C}	185.6 ± 8.1^{D}	< 0.001 † HS
Range	169.0- 320.0	158.0 – 272.0	125.0 – 190.0	161.0 – 198.0	
Different latters denote to the significant differences at p< 0.05					
Triglyceride mg/dl					
Mean± SD	196.0± 70.31 ^{A}	182.3± 54.86 ^{A}	127.33± 19.9 ^{B}	126.83± 17.4 ^{B}	< 0.001 † HS
Range	90.0- 410.0	70.0 –315.0	70.0 – 160.0	85.0 – 125.0	
Different latters denote to the significant differences at p< 0.05					
HDL mg/dl					
Mean± SD	40.23± 6.49^{A}	40.16± 5.83 ^{A}	44.53± 4.74 ^{B}	48.20± 6.89^{B}	< 0.001 † HS
Range	30.0- 55.0	31.0 –52.0	38.0 – 52.0	29.0 – 64.0	
Different latters denote to the significant differences at p< 0.05					
VLDL mg/dl					
Mean± SD	39.20± 14.06 ^{A}	36.46± 10.97 ^{A}	25.46± 3.99 ^{B}	25.06± 3.87^{B}	< 0.001 † HS
Range	18.0- 82.0	14.0 –63.0	14.0 – 32.0	16.0 – 31.0	
Different latters denote to the significant differences at p< 0.05					
LDL mg/dl					
Mean± SD	146.93± 30.29 ^{A}	126.26± 24.29^{B}	93.06± 15.42 ^{C}	111.50± 10.5^{D}	< 0.001 † HS
Range	95.0- 228.0	86.0 –182.0	53.0 – 114.0	84.0 – 131.0	
Different latters denote to the significant differences at p< 0.05					
Blood urea mg/dl					
Mean± SD	53.73± 13.77 ^{A}	39.83± 9.18 ^{B}	32.86± 8.06 ^{C}	30.83± 6.32 ^{C}	< 0.001 † HS
Range	33.0- 85.0	26.0 –65.0	19.0 – 44.0	19.0 – 41.0	
Different latters denote to the significant differences at p< 0.05					

S. creatinine mg/dl					
Mean± SD	1.22± 0.36 ^{A}	1.11± 0.37 ^{A}	0.82± 0.21 ^{B}	0.93± 0.126 ^{B}	< 0.001 † HS
Range	0.7- 1.9	0.5 –2.2	0.5 – 1.2	0.7 – 1.2	
Different latters denote to the significant differences at p< 0.05					
Total protein g/l					
Mean± SD	63.26± 3.75^{A}	59.33± 6.08 ^{B}	62.00± 3.60 ^{AB}	64.53± 3.26 ^{A}	< 0.001 † HS
Range	57.0- 70.0	32.0 –66.0	58.0 – 69.0	58.0 – 70.0	
Different latters denote to the significant differences at p< 0.05					

n: number of cases; SD: standard deviation; †: one way ANOVA; ¥: Chi-square test; HS: Highly significant at P ≤ 0.001; NS: not significant at P ≤ 0.05.

The mean levels were higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant (P < 0.001). The mean cholesterol levels were higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant (P < 0.001). The mean TG levels was higher in Acute coronary syndrome patients with toxoplasmosis in comparison with other groups and the difference was highly significant (P < 0.001). The mean Urea levels of serum creatinine highly significant increase in Acute coronary syndrome patients with toxoplasmosis in compared to other groups (P < 0.001).

Several biomarkers are utilized as indications of cardiovascular disorders. A biomarker is a feature that is examined and analyzed as a hallmark of a pathological activity. Having high levels of triglycerides (TG) or total cholesterol (TC) is linked to heart disease, and having high levels of low-density lipoprotein cholesterol (LDL-C) is a key risk factor for cardiovascular malfunction. Increases in both systolic and diastolic blood pressure may lead to arterial obstruction and an increased demand on the heart, both of which may lead to myocardial disease. C-reactive protein (CRP) is a pro-inflammatory cytokine-stimulated acute-phase protein that is used as a predictor of systemic inflammatory processes and cardiovascular conditions (Atkinson et al., 2001; Avan et al., 2018; Castro et al., 2018; Nordestgaard & Varbo, 2014; Stevens et al., 2016).

Toxoplasma infection has been linked to cardiovascular disorders according to recent research. However, the investigation did not include people from the United States. Recent research has linked T. gondii IgG antibodies to chronic inflammation and vascular damage indicators including C-reactive protein. The study by (Babekir et al., 2021) found that elevated SBP, TG, GGT, and FG, and decreased HDL, were all related with positive T. gondii IgG antibody. The results of (Babekir et al., 2021) study demonstrated the favorable connection between T. gondii illness and a jump in the amount of LDL, TG, and GGT and an important unfavorable connection with the level of HDL after controlling for age (Khademvatan et al., 2020).

Following the protocol established by the American Heart Association for CVH, (Babekir et al., 2021) conducted in-depth analyses of each individual biomarker and aggregated the results into an overall cardiovascular biomarkers index (OCBI). HDL, GGT, and CRP are some of the other biomarkers that were recently included to this OCBI. Due to its positive correlation with CVD risk and negative association with Toxoplasma, HDL was included in the index as a biomarker. Previous research has connected GGT and CRP to cardiovascular health.

Predictive models including OCBI and Toxoplasma data demonstrated their link. Even after controlling for socioeconomic status, smoking status, and body mass index, this correlation remained. Toxoplasma may play a role in cardiovascular dysfunction; however, it is important to continue

focusing on reducing risk factors for cardiovascular disease such as eating habits, physical activity, genetics, and other primary illnesses. Mechanistic mechanisms caused by consumption appear to possibly cause cardiovascular disease, but other, perhaps less important contributing variables, such as Toxoplasma, must be examined as well (Kreutzer et al., 2019; Pizzino et al., 2017).

Complex mechanisms linking T. gondii infection and cardiovascular dysfunction are hypothesized, but essential patterns are evident. T. gondii infection is associated with elevated levels of oxidative stress and inflammation, both of which are detrimental to cardiovascular health. Nuclear factor kappa B (NF-kB), interferon regulatory factors (IRFs), and mitogen-activated protein kinases (MAPKs) all play key roles in the inflammation process. IL12, IL1, IFN I and II, and TNF are all induced in large part by these three pathways (Akira et al., 2006; Mogensen, 2009).

Egorov et al. (Egorov et al., 2021) detected that latent T. gondii infections can affect vascular damage and inflammatory processes related signatures represent primary pathophysiological procedures that may be set off by the spontaneous breakdown of tissue cysts and expulsion of bradyzoites within intermediate hosts. This activates the immune system, which eliminates the expelled bradyzoites, in those with a healthy immune system. Vascular endothelial cells release vascular cell adhesion molecule 1 VCAM-1 and ICAM-1 into the bloodstream in response to inflammation (Furtado et al., 2012; Tomasik et al., 2016). They play an important role in leukocyte adhesion and transmigration through the vascular endothelium. T. gondii infected bovine endothelium cells were shown to have increased expressions of ICAM-1 and VCAM-1 in vitro. In the early stages of infection, the parasite has been demonstrated to employ ICAM-1 to get through the blood-brain barrier and other endothelial barriers. It is not yet known how ICAM-1 contributes to the latent infection stage. Serum levels of VCAM-1 are increased in infected animals, and regulating T. gondii infection is impossible without it. Atherosclerosis has been associated to higher amounts of these adhesion molecules for quite some time now (Jitender P. Dubey et al., 2016; Egorov et al., 2018).

Similar to the previous study, (Egorov et al., 2021) found that CMV IgG serology or the severity of anti-CMV IgG reactions was linked with increased levels of VCAM-1, ICAM-1, and CRP. There may be overlapping molecular pathways that lead to adverse health outcomes when CMV and T. gondii infections have both been related with psychiatric problems. However, the precise cause-and-effect mechanisms that link chronic inflammation to mental problems have yet to be determined. Previous studies have shown that T. gondii infection leads to neuronal damage. While there is mounting evidence that T. gondii infection leads to behavioral abnormalities, neurological deficits, and mental illnesses, the precise molecular pathways underlying these effects have yet to be elucidated. Exposure to common air pollutants has been shown to raise blood levels of atherosclerosis (Tyebji et al., 2019).

Conclusion

In conclusion, the findings of this study provide valuable insights into the relationship between Toxoplasma infection and acute coronary syndrome (ACS), as well as the potential influence of blood groups on Toxoplasma infection. The results from Table 1 indicate a significantly higher prevalence of Toxoplasma infection among ACS patients compared to the healthy control group. This suggests a potential association between Toxoplasma infection and the development or progression of ACS. These findings are consistent with previous studies linking chronic infections, including Toxoplasma infection, to cardiovascular diseases. The blood group type may not be a significant factor influencing susceptibility to Toxoplasma infection in the study population. The distribution of blood groups did not show any significant differences between patients with and without Toxoplasma infection, as well as between healthy individuals with and without Toxoplasma infection. These results are in line with some previous studies, although the relationship between blood groups and Toxoplasma infection may vary across different populations.

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