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ORIGINAL ARTICLE

Investigation of Herpes Simplex Virus-2 (Hsv-2) Infection in Coronary Artery Disease Patients (CAD) in Population from Iran

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ABSTRACT
Recent studies have suggested relationships between herpes simplex virus(HSV-2)infection and coronary artery disease (CAD). Presented study investigated the association between the HSV-2immunoglobulin G (IgG) seropositivity, in angiographically diagnosed coronary disease blood. In order to evaluation of Hsv-2 Infection In CAD Patients blood samples were obtained from 193 CAD patients admitted for coronary angiography because of suspected coronary heart disease. Lipid parameters and blood glucose level (fasting blood glucose and random blood glucose) were determined. Of the 193 CAD patients, 192(99.49%) were positive by an ELISA method for herpes simplex virus-2 antibodies IgG and 1 (0.51%) were negative for Hsv-2IgG. When IgG antibodies were considered, there was significant correlation between biochemical parameters and seropositivity of HSV-2 antibody in CAD patients. In conclusion, HSV-2 infection is more common in CAD patients. Chronic HSV-2 infection may be associated with the development of atherosclerotic coronary disease and viral treatment have effective role in control of advanced heart problems.
Keywords: Coronary Artery Disease, herpes simplex virus-2, Iran

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INTRODUCTION

Herpes simplex virus (HSV) also known as human herpes virus 1 and 2 (HHV-1 and HHV-2) infection is one of the most common latent viral diseases worldwide. HSV-2 is large double-stranded
DNA virus, which belong to a subfamily of the Herpesviridae family. HSV-2 can be spread through contact with body fluids and infected area of the skin during re-activations of the virus., indeed infected person can be spread it when producing and infusing the virus in their body.HSV-2 are contagious and transmitted across epithelial mucosal cells, after Skin intervals, then migrate to nerve tissues. HSV-2 as neurotropic and neuroinvasive virus, becoming *latent* infection that lives in the cell bodies of neurons and cause persist infection [1-7]. Herpes viruses establish lifelong infections, and the virus cannot yet be eradicated from the body. Symptoms of herpes simplex virus infection include, genital mucous membranes lesions. HSV-2 infection may be symptomatic or asymptomatic, sometimes cause very mild or atypical symptoms. HSV-2 typically found in the lumbosacral ganglia and cause genital lesions [8, 9]. Genital herpes is a common sexually transmitted infection, caused by the herpes simplex virus 2 . A woman who has a primary episode in the last trimester, especially in the last four to six weeks, may be treated to reduce the viral load. The rationale for serological testing is to identify asymptomatic HSV2 infection. Until recently, HSV serology was unhelpful because it could not accurately differentiate antibodies to HSV-2 (almost exclusively as a result of genital herpes) from HSV-1 (predominantly generated in response to an orolabial infection). But previous studies have shown that virtually all patients with HSV-2 antibody have genital herpes [10-14]. HSV-2 scope from immune system through

interference with antigen presentation phenomenon with MHC class I on the cell surface, that block the antigen transport process [10]. The main effect of this block is inhibition of cell-mediated immune response via activation of cytotoxic T-lymphocytes against virally-infected cells, that allowing the virus to survive for a protracted period in the host [14]. HSV-2 could be a non aligned risk factor for cardiovascular disease and myocardial infarction [15]. Due to HSV infection thrombogenic and atherogenic changes to host cells occurred, so because the generation of thrombin via the essential phospholipid and tissue factor activities on its surface [17-21]. Coronary artery disease (CAD) is one of the main causes of Death world width. Coronary artery disease, usually caused by the formation of plaques in the arteries which blocked these arteries and reduce blood flow to the heart muscle, then the heart muscle is deprived of oxygen. the Several studies demonstrated Inflammation has a significant role in CAD [18-25], so viral infections as a infective factor could be prepare susceptibility to atherosclerosis and related complications .on the other hand Infections have been correlated with an higher prevalence of atherosclerosis [19-23]. CAD may be related to inflammation, and inflammation is one of the symptoms of HSV-2 infection. immune response involve in HSV-2 infection has essential effect in the pathogenesis of coronary artery disease, Since some infective agents have been recognized in atherosclerosis plaques, indeed could be Assumed that it could engaged in vascular inflammation by persistent infection or by immunity response related injury [19,20,22-27]. HSV-2, which has been identified as a potential cardiovascular pathogen and involved in carotid disorder, CAD and atherosclerosis that is related to risk of cardiovascular conflicts. Hence In this study we investigated the Probable relationships between HSV-2 infection and CAD.

MATERIAL AND METHODS

Our cohort study performed in population included 192 patients (mean age 57.43 ±11.078 years) with CAD who coronary angiography and had a positive angiogram. All patients were examined by a cardiologist .this study performed during September 2013, until May 2014, in Uremia Sayidoshohada hospital, Iran. All patients were tested for HSV-2 specific antibody (IgG).For HSV-2seroprevalence, plasma antiHSV-2IgG were examined by ELISA method. Major risk factors of CAD (hypertension, hyperlipidemia, diabetes, obesity and smoking) evaluated. ELISA. Plasma total triglycerides, cholesterol, low (LDL) and high density lipoproteins (HDL), fasting blood sugar (FBS), random blood sugar (BS) were determined. Satisfaction forms that detail of study listed in, were collected from all patients, and then by each cases signed. For each patient's Blood samples (5 ml) were drawn. After blood collection, serum isolated andused to special analysis. Our subject's were examined for HSV-2 specific antibodies. Antibodies specific for the HSV-2 were detected by immunoassay analysis. Serum was analyzed for specific positive IgG antibodies by enzyme-linked-immunosorbent assay (ELISA), as per the manufacturer's instructions. (diapron, Rom, Italy). Lipid profile includes Plasma total triglycerides, cholesterol, and high density lipoproteins (HDL), and glycemic level as FBS: (Fasting blood sugar), and blood sugar (BS), was measured via spectrophotometry and commercially available kits (Pars Azmoun, Iran). The following Studied parameter was Inflammatory Marker; c reactive protein (CRP) thatwas in the serum was determined by CRP latex kit as qualitative method (ATLASC REACTIVE PROTEIN (CRP) LATEX KIT). Statistical analyses by using SPSS version 21 done. Statistical procedures for quantitative variables wereT- test to determination of frequency (percentage %) and Comparison between serum parameters were determined using independent t- test. For evaluation of the mean lipids concentrations and other biochemical parameter and significant difference between patients ANOVA/Chi-square test were used. data presented as mean ± SD for studied variables and significant differences was $P < 0.05$.

RESULT

A total of 193 studied populations with coronary artery disease and positive coronary angiography in age range of the 29 to 95 years were evaluated for IgG antibody against HSV-2.data showed Mean age of the CAD patients was 57.43 ±11.078 years. Demographic and biochemical finding of the studied population are presented in Table 1.Also data based on evaluation of Hsv-2 antibody and CRP tests that detected as seronegative and seropositive presented in table 2.

Variables are presented as Mean± Std. Deviation, TC: Total cholesterol, TG triglyceride, BS: blood sugar, FBS: fasting blood sugar, LDL: low density lipoprotein cholesterol, HDL: high density lipoprotein cholesterol.

Table 1: Demographic and biochemical parameters of patients

N=193	Mean± Std. Deviation	Std. Error Mean
Age	57.43 ±11.078	.799
HDL	37.06 ±19.727	1.718
LDL	47.27 ±51.372	3.883
TG	180.37 ±104.265	7.882
TC	125.62 ±67.385	7.307
BS	123.46 ±101.199	7.739
FBS	108.80 ±54.792	4.582

The prevalence of IgG antibodies against HSV-2 was high in both genders. There was no significant differences was observed in prevalence of IgG antibodies against hsv-2 between males and females (p>0.05)

According to our data, HSV-2 infection had a high prevalence in our cases with coronary Artery disease. Results from the antibody detection tests against HSV-2 were determined as seronegative or seropositive presented in Table 2.

Table 2: HSV-2 frequency distribution in patients with coronary artery disease

Percent%	frequency	HSV-2 antibody test
99.49	192	seropositive
0.51	1	seronegative
100.0	193	total

Results from the CRP test were considered as seronegative or seropositive based on the results shown in Table 3.

Table 3.CRP frequency distribution in patients with coronary artery disease

Percent%	frequency	CRP
71.01%	98	seropositive
28.09%	40	seronegative
100.0%	138	total

In multiple logistic regression analysis, of the infectious agent (HSV-2), there was significant correlation between seropositivity of HSV-2 antibody and biochemical parameters, in our population. Results shown,HSV-2 antibody positivity was significantly correlated with CAD (95% CI, p < 0.05) and TG (95% CI, P< 0.05) and CRP (95% CI, P< 0.05) and FBS level (95% CI P<0.05), BS level (95% CI P<0.05), LDL-c (95% CI P<0.05).(Table 4)

Table 4: Correlation of with IGg antibody against hsv-2 with, serum triglycerides (TG) LDL-c, Fasting Blood Sugar FBS, Triglyceride TG, CRP;C reactive protein., in patients

	CRP	FBS	LDL	HDL	TG	BS
Pearson correlation	0.627	0.270	0.360	0.16	0. 793	0.210
Significant	Sig	Sig	Sig	NSig	Sig	Sig
	P<0.05	<0.05	<0.05	>0.05	<0.05	<0.05

Sig: Significant
Nsig: Non significant
P v:P value

DISCUSSION AND CONCLUSION

Atherosclerosis is one the main reason of cardio-vascular Disorders (CAD).On theother hand hypertension, hypercholesterolemia, diabetes, smoking; environmental factors and hereditary factors are the major risk factor for CAD. Several infections such as viral infections can be as risk factors of atherosclerotic diseases [25,26]. Coronary artery disease (CAD) is one of the main causes of Death worldwide that usually can be due to the formation of plaques in the arteries and these artery blockage and ultimately artery damages. Inflammation has a noticeable effect in progression of CAD [18, 24-25]. Different surveys Reported higher prevalence Of HSV-2 infection in CAD patients, while other study do

not. Herpes simplex virus (HSV), human herpes virus 2 (HHV-2) infection is a common latent viral infection worldwide in both gender.

HSV-2 becoming latent infection that remain and grows then causes persistent recurrent inflammation. The main symptom of genital herpes (HSV-2) is an outbreak of sores or blisters in the genital area, and sometimes around bottom or on thighs. In about 90% of cases, neonatal herpes is transmitted when an infant comes into contact with HSV- 2 in the birth canal during delivery. There is a high risk of transmission if the mother has an active outbreak, because the likelihood of viral shedding during an outbreak is high. There is also a small risk of transmission from asymptomatic shedding (when the virus reactivates without causing any symptoms) [10-13]. In fact our studies investigated the association of infection with HSV-2 infection and CAD, indeed Major aim of our study was to study the prevalence of HSV-2 IgG between coronary artery disease patients. The HSV-2 IgG seropositivity were 99.4%% (192 patients) of CAD. There was high seroprevalence of hsv-2 infection in patients with CAD. With evaluation of inflammatory parameter (CRP), data shown CRP positive results were 71.01% (98 patients) in CAD patients. In further study of our subjects, there was significant positive correlation between HSV-2 infection and CAD. We can suggest that patient with positive report of IgG antibody against HSV-2 is at higher risk for CAD and their complication. Indeed Hsv-2 infection have significant distribution between our population .in study of CAD risk factor included lipid profile and hypertension and smoking ,there was significant relationship between this infectious agent and some parameters of lipid profiles such as triglyceride, LDL-C, and inflammatory parameter (CRP)($p<0.05$)and elevated blood sugar,($P<0.05$) that proven in this study . Therefore HSV-2IgGseropositivity (HSV-2 infection) could be influences some lipid profile changes and also progress systemic inflammation response that may be due to activation of immune responses. The result of our study showed that Coronary Artery Disease patients had higher frequency of positive anti- HSV-2antibody. Therefore, we suggest that probably there is a relationship between HSV-2 infection and coronary artery diseases.

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