Original Article

Hepatitis B Virus Infection and the Risk of Coronary Atherosclerosis

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Abstract

Introduction: Many studies have reported on the association between human coronary artery disease (CAD) and certain persistent bacterial and viral infections. Currently, it is unclear whether hepatitis B virus infection is associated with the risk of the atherosclerosis. The aim of this study was to investigate the possible association between hepatitis B virus infection and angiography-proven CAD. Materials and Methods: Sera from 5004 patients who underwent coronary angiography were tested for hepatitis B surface antigen (HBsAg) by enzyme-linked immunosorbant assay at Madani Heart Hospital, Tabriz University of Medical Sciences, Iran. Results: Our study population comprised 66% male and 34% female, with an age range of 36 to 86 years. The prevalence of HBsAg positivity tended to be higher in CAD patients than in those without CAD (3.28% versus 2.17%), but the difference was not statistically significant. Conclusion: Our results suggest that hepatitis B virus infection is not associated with coronary atherosclerosis in this population.

Ann Acad Med Singapore 2008;37:913-5

Key words: Atherosclerosis, Coronary artery disease, Hepatitis B virus

Introduction

Coronary artery disease (CAD), also called coronary heart disease, is the leading cause of death for both men and women. CAD is usually caused by atherosclerosis.[1] Atherosclerosis (the hardening of the arteries) is the most common form of arteriosclerosis, in which the walls of arteries become thicker and less elastic. Through deposits along the arteries that contain calcium, fatty material accumulates under the inner lining of arterial walls, causing them to narrow and eventually lead to the impairment of blood flow. Atherosclerosis is a complex histopathological process.[2] Coronary angiography is the most accurate method for making a diagnosis of CAD.[3] Risk factors for atherosclerosis include age, sex, smoking, diabetes mellitus, hypercholesterolaemia, hypertension, family history and elevated C-reactive protein (CRP) levels.[3,4] Inflammation plays a central role in CAD.[5] Epidemiological studies indicate that infectious agents may predispose patients to atherosclerosis and adverse clinical events. Infections have been associated with an increased risk of atherosclerosis.[6-12] At the beginning of the 1970s, the monoclonal hypothesis was first proposed, suggesting a potential role for viral inflammation in the atherosclerotic process.[13] Several experimental studies have suggested that immune mechanisms have important roles in the pathogenesis of atherosclerosis.[11] Since some pathogens have been identified in atherosclerosis plaques, it has been hypothesised that it may precipitate vascular inflammation by either persistent infection or by immunity-related injury.[14] Recently, the association of atherosclerosis and hepatitis B virus (HBV) infections has been reported.[9-12] The aim of this study was to evaluate the association between HBV infection and the risk of atherosclerosis in northwest Iran.

Materials and Methods

Data of 5004 patients of both genders were collected at Madani Heart Center, Tabriz, Iran. This cross-sectional study consisted of subjects who had undergone coronary angiography due to chest pain or non-invasive tests compatible with myocardial ischaemia between 2005 and 2006. Sociodemographic characteristics, medical history on hypertension and diabetes, and information regarding smoking habits were analysed by a computer program. Coronary angiography was performed in a cardiac

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catheterisation laboratory. Electrocardiogram (ECG) electrodes were placed on the patient's chest and an intravenous line was inserted. A local anaesthetic was injected into the site where the catheter was to be inserted. The cardiologist inserted a catheter into a blood vessel and guided it into the heart. A contrast dye was then injected to make the heart visible on X-ray cinematography. Venous blood samples were collected under standardised conditions after an overnight fast and centrifuged within 15 minutes (3000 g for 10 minutes). Serum fasting blood sugar, cholesterol, triglyceride, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and very-low-density lipoprotein (VLDL) were measured with autoanalyser Cobas Mira. HBsAg were determined by enzyme-linked immunosorbant assay (Hepanestika® HBsAg Uniform II, Biomerieux).

Statistical analysis was performed using ANOVA test, X^2 test, and univariate and multivariate logistic regression analyses using SPSS software, version 13. All probability values were 2-tailed and values <0.05 were considered statistically significant.

Results

Our study population included 4499 patients (1358 females, 3141 males), with the average age of 57.71 ± 11.09 years and angiographic documentation of CAD (>50% stenosis). A control group of 505 patients (168 females, 337 males) was also recruited; these patients were hospitalised in the same centre for reasons other than suspected CAD, and had angiographically-documented normal coronary arteries. Both cases and controls did not differ according to gender and sex distribution. Characteristics of the patients and the traditional risk factors of CAD are summarised in Table 1. Comparisons with regard to cardiovascular risk factors revealed that cases were high among current smokers who had higher systolic blood pressure, and cholesterol and diabetic levels than controls. The prevalence of positive findings for HBsAg was 2.15% at this region. Those with positive tests for HBsAg were older. Of the 5004 subjects, 159 patients (3.17%) were diagnosed as carriers of HBV. The prevalence of HBsAg positivity tended to be higher in CAD patients than in non-CAD patients (control group) (3.28% versus 2.17%), but the difference was not statistically significant ($P = 0.428$) (Table 2). There was no independent association between HBsAg positivity and the risk of atherosclerosis.

Table 1. Characteristics of Patients with Traditional Risk Factors of Coronary Artery Disease and Hepatitis B Virus Infection

Variable	OR (95% CI)	*P*
Male	1.2 (0.9-3.0)	0.016
Age	1.5 (1.2-2.8)	0.001
Hypercholesteremia	1.1 (0.5-2.6)	0.002
Hypertriglyceridaemia	1.1 (0.55-2.1)	0.064
CRP	1.6 (0.9-2.3)	0.103
Hypertension	1.4 (0.6-3.0)	0.045
Diabetes	1.9 (1.3-3.1)	0.034
Smoking	1.8 (1.7-2.3)	0.031
HBsAg	1.5 (0.8-2.8)	0.428

Hypercholesteremia: total cholesterol >260 mg/dL;
Hypertriglyceridaemia: triglyceride >160 mg/dL;
Hypertension: blood pressure 140/90
95% CI: 95% confidence interval; CRP: C-reactive protein; OR: odds ratio

Table 2. Coronary Artery Disease (CAD) in Patients with and without Hepatitis B Virus Infection

		CAD		
		Yes	**No**	**Total**
HBsAg	+	148	11	159
	-	4351	494	4845
Total		4499	505	5004

Discussion

The aetiological complexity and the remarkable epidemiological and social importance of atherosclerosis have given rise to extensive research on its pathogenesis. Many patients with CAD lack conventional risk factors, suggesting that there are additional unidentified factors contributing to vascular injury.[14] However, one of the most interesting developments in recent years has been the idea that infective agents may induce a pro-inflammatory effect and play a crucial role in atherosclerosis.[6,7,15-19]

Recently, Ishizaka et al[12] reported that the positivity for HBsAg was associated with carotid atherosclerosis. Tomiyama et al[11] showed that HBsAg positivity was not associated with atherosclerosis. However, others failed to show any significant association between HBV infection and atherosclerosis.[4,20,21]

In this study, no association was found between HBV infection and coronary atherosclerosis. Differences in study design, frequency of individuals with chronic HBV infection, and regional differences may explain the differing results. Currently, there are little data on the association between HBV infection and atherosclerosis. Since serologic markers of HBV infection are guides to the natural course of disease, no concrete evidence has been found to support the infection of HBV in endothelial cells in HBsAg carriers. Thus, we examined one widely used serologic marker (HBsAg) instead of more sensitive HBV-DNA detection in endothelial cells, with the hypothesis that circulating HBV-associated antigens might be the risk factors for

atherosclerosis. In our study, no complete data were available with regard to polymerase chain reaction (PCR) findings and anti-HBV antibodies. Thus, we could not fully exclude the effects of HBV infections on the risk of atherosclerosis. Although the HBV-DNA detection test is not practical for general health screening tests from an economic standpoint, the link between HBV-DNA positivity and atherosclerosis should be clarified in future studies. Recent studies have shown that the pathogen burden predicts the presence and severity of CAD more strongly than any single pathogen.[14,22] Researchers have suggested that the composite effect of multiple pathogens, rather than any single organism, is the cause of the development of endothelial dysfunction. This study dealt with a single organism (HBV), but it is recommended that research on multiple organisms should be carried out in future. We concluded that there was no association between HBV infection and atherosclerosis in this population. Screening for HBV is not recommended in preventing atherosclerotic disease.

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