FULL LENGTH ARTICLE

Correlation of hyper-homocysteinemia with coronary artery disease in absence of conventional risk factors among young adults

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Objective: Coronary artery disease is major cause of mortality and morbidity. Homocysteine has long been postulated as an underlying factor for atherosclerosis leading to coronary artery disease, yet its role in young patients is uncertain. This study was aimed to analyze the correlation between plasma homocysteine and coronary artery disease among young adults in the absence of conventional risk factors.

Methods: It was a case-control study carried out at Rehman Medical Institute, Peshawar, Pakistan from October 1, 2016, to September 30, 2017. Universal sampling technique was adopted and 158 participants were included. A total of 30 participants were in the control group and 128 were in the patient group, who had moderate to severe stenosis in either single or multiple major coronary arteries on coronary angiography and aged <40 years.

Results: Cases and controls had similar characteristics but differed significantly in serum homocysteine concentration. In the control group, the mean plasma homocysteine concentration of 6.3 (þ2.05) µmol/L and in the patient group a mean plasma homocysteine concentration of 44.5 (þ14.01) µmol/L was observed. All the patients with moderate to severe stenosis in single or major coronary arteries had raised plasma homocysteine concentrations. Among 128 patients, 15 (11.7%) had moderate increase, 109 (85.2%) had intermediate increase, and four (3.1%) had severe increase in plasma homocysteine levels. Single vessel coronary artery disease was observed in 118 (92.2%) patients, whereas 10 (7.8%) had more than one major coronary artery involvement.

Conclusion: Hyper-homocysteinemia has positive correlation with coronary artery disease among young adults in the absence of conventional risk factors.

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Introduction

One third of global deaths are caused by cardiovascular events [1]. In developed countries such as the United States, >600,000 deaths annually are attributed to cardiovascular diseases [2]. Ischemic heart disease is the biggest culprit contributing to the major cause of mortality from heart diseases [3]. Atherosclerosis is the hallmark of ischemic heart disease which is characterized by narrowing or blockage of coronary arteries supplying all the nutrients and oxygen to the heart [4]. Coronary angiography is the gold standard for detecting coronary artery disease [5].

Homocysteine accelerates atherosclerosis by increasing the prothrombotic factors XII and V and decreasing the antithrombotic factors along with endothelial derived nitric oxide. Hyper-homocysteinemia also inculcates direct endothelial cell damage, which leads to smooth muscle cells hyperplasia, contributing to occlusion or narrowing of the vessels. Increased plasma levels of homocysteine contribute to cardiac morbidities and it has positive association with hypertension [6]. Aspirin resistance is also increased with high levels of homocysteine in the blood [7]. Therefore, homocysteine has been thought of as an independent risk factor contributing to coronary artery disease and the Framingham Risk score has been challenged [8]. Low levels of vitamin B12 and high serum concentration of homocysteine have been associated with coronary artery disease in Asians and investigated by two different studies in the Indian population [9,10]. Homocysteine is a modifiable risk factor and folic acid supplementation improves the endothelial dysfunction caused by high serum concentration of homocysteine [11].

The vascular toxicity of hyper-homocystenemia is well established, yet we have limited evidence regarding the isolated effect of hyper-homocystenemia on coronary artery disease in the younger population in absence of cumulative and synergistic effect of conventional strong risk factors. This study aimed to analyze the correlation of serum homocysteine and coronary artery disease in young adults in the absence of conventional risk factors. As it is a modifiable risk factor, targeting it will decrease both the cardiovascular mortality and morbidity.

Materials and methods

This study was carried out at the Cardiology Department of Rehman Medical Institute (RMI), Peshawar, Pakistan. RMI is a specialized tertiary care hospital providing modern state of the art facilities to patients from across the province and neighboring countries. It was an observational case-control study carried out for a period of 12 months from October 1, 2016, to September 30, 2017. A total of 158 participants were included; 128 participants in the patient group and 30 participants in the control group.

In the patient group, a universal sampling technique was adopted and every patient who had angiographic evidence of moderate to severe stenosis in single or multiple major coronary arteries on coronary angiography aged <40 years and >25 years was included. In the control group, random sampling from the general population was done having features similar to the participants of the patient group. Patients from each sex, different ethnic backgrounds, multiple geographic locations, and different socioeconomic statuses were part of the study population in both groups.

All those participants who had mild stenosis in coronary arteries, were using antihypertensive medications including calcium channel blockers, beta blockers, diuretics, or had a blood pressure measurement of >140 mmHg systolic and >100 mmHg diastolic, were using antidiabetic medications including oral antidiabetics or insulin or had a random blood glucose level of >200 mg/dL, fasting blood glucose level of >126 mg/dL or HbA1c of >6.5%, were active smokers and smoked more than one cigarette daily, had familial hyperlipidemia or dyslipidemia, or had blood cholesterol level >250 mg/dL, taking drugs such as antidepressants (S-adenosyl methionine), methotrexate, phenytoin, carbamazepine, 6-azauridine triacetate, recently undergone general anesthesia or were exposed to nitrous oxide were excluded from the study population.

In an EDTA tube, 5 mL fasting blood sample was collected under aseptic technique, having 8

Abbreviations

RMI	Rehman Medical Institute
FPIA	Fluorescence Polarization Immunoassay
CAD	Coronary artery disease
QCA	Quantification of coronary atherosclerosis
SVCAD	Single vessel coronary artery disease
DVCAD	Double vessel coronary artery disease
TVCAD	Triple vessel coronary artery disease
BMS	Bare metal stent
PCI	Percutaneous Cutaneous Intervention