

Hyperhomocysteinemia in Patients with Coronary Artery Disease

Adina Shamsi, M. Zamir Ahmad, Sadia Amir and Qurat-ul-Ain

Background: Pakistani people belong to an ethnic group, which has the highest rate of coronary artery disease. Hyperhomocysteinemia arising from impaired methionine metabolism is associated with premature cerebral, peripheral and coronary vascular disease. This study was carried out to determine the association of hyperhomocysteinemia with coronary artery disease.

Method: The study was conducted at the Department of angiography Punjab Institute of Cardiology. Fasting venous blood sample was obtained from 60 patients with coronary artery disease and thirty controls. Plasma was analysed for total Homocysteine level using Bio-Rad EIA microtitre method.

Result: Plasma total Homocysteine level in cases was significantly higher as compared to controls.

Conclusion: Coronary artery disease was associated with hyperhomocysteinemia in our patients and this variable may strongly predispose to coronary artery disease in our country.

Key words: Hyperhomocysteinemia, risk factor, coronary artery disease.

Introduction

Cardiovascular diseases are a major cause of mortality all over the world and its global incidence is increasing.¹ Conventional risk factor such as hyperlipidemia, hypertension, obesity and cigarette smoking do not account for all cases in this epidemic. So there is a need to identify additional risk factors for coronary artery disease.² Factors leading to hyperhomocysteinemia include old age, male gender, nutritional deficiency of vitamin B₁₂, vitamin B₆ and folic acid.³ In 1969 McCully made the clinical observation linking elevated. Subsequent investigations have confirmed McCully's hypothesis and it is now clear that hyperhomocysteinemia is an independent risk factor for atherosclerosis in coronary, cerebral and peripheral vasculature.⁴ Although severe hyperhomocysteinemia is rare, but mild hyperhomocysteinemia occurs in approximately 5-7% of general population.⁵ Patients with mild hyperhomocysteinemia have none of the clinical signs of severe hyperhomocysteinemia and are asymptomatic until third or fourth decade of life when premature coronary artery disease develops, as well as recurrent arterial and venous thrombosis.⁶ Homocysteine is a thiol containing amino acid and is not a building block for proteins. Homocysteine is not a normal dietary constituent and the sole source of homocysteine is essential amino acid methionine.⁷ Hyperhomocysteinemia is defined as a total homocysteine level of >90th percentile of control population. Its level ranges from 5-15 µmol/l in fasting state and in most studies a level of 15 µmol/l is >90th percentile of control population.⁸ Its level

impaired in hypothyroidism and genetic deficiency of enzymes like cystathionine β synthase.⁹ This study was conducted with the objective to determine the association of homocysteine and other risk factors with coronary artery disease.

Method

The proposed study was a non-interventional comparative study carried out at the Department of Angiography, Punjab Institute of Cardiology from July 2003-Dec2003. The study population included 60 stable coronary artery disease patients of both sexes between the age group 35-60 years. Only those patients were selected as cases who were angiographically verified as having coronary artery disease. Subjects with renal failure, having thyroid disease, megaloblastic anemia and diabetes mellitus were excluded from the study. An informed consent was obtained from each patient. The data collection for various groups was standardized through the use of similar standard methodology, protocol and procedure using a standard questionnaire. The questionnaire provided information about occupation, smoking habit, medical history of cardiovascular disease, hypertension and family history of coronary heart disease. Patients were categorized as hypertensive if they were on antihypertensive treatment.

Specimen Handling and Storage:

A 5ml venous sample was obtained after informed consent from antecubital veins of patients with coronary artery disease and controls into a

Vacutainer tubes one with EDTA (for preparation of plasma) after an overnight fast of 10-12 hours. The plasma was separated within an hour and stored at -20 °C until analysed for Homocysteine. Plasma was analysed for total Homocysteine level using Bio-Rad EIA microtitre method.

The data was entered and analysis was performed with the statistical package SPSS software version 10 for Windows.

Results

A total of 90 subjects were studied, 76 were males and 14 were females. The average age was 43.95 years.

Table 1 compares mean total homocysteine level between coronary artery disease cases and controls.

Table 2 shows the comparison of various risk factors between cases and controls.

Table 1: Mean Total Homocysteine Levels in Cases and Controls

Study Group	No.	Mean SD	t-test
Cases	60	15.21 ± 2.67	p<0.01
Controls	30	10.88 ± 1.88	

Table 2: Comparison of various risk factors between cases and controls

Risk Factors	Cases	Controls	Chi-square
Hypertension	20	10	p=1
Smoking	31	44.4	p<0.05
Hyperlipidemia	17	4	p=.11
H/O CHD	33	11	p=0.10

Discussion

Various risk factors are known to predispose to coronary artery disease. These factors were recorded in our study such as history of hypertension smoking, history of hyperlipidemia, family history of coronary heart disease and a relatively new risk factor plasma total homocysteine. Akosh et al have reported that history of smoking was independently associated with premature coronary heart disease and they found a higher percentage of smokers with ischaemic heart disease than controls¹⁰. It is shown by a study done by Gensini that smoking is responsible for 29% of total deaths from coronary heart disease¹¹. In our study the percentage of smokers is significantly high (p<0.05) in patients with coronary artery disease when compared to control samples. In our study we report no significant difference between history of hypertension, history of hyperlipidemia, family history of coronary heart disease in cases and control subjects. Stampfer et al and Clark et al reported in their studies that increased levels of plasma Homocysteine are common in patients with myocardial infarction and vascular disease^{12,13}.

Similar high levels of plasma homocysteine have been reported by studies done in Pakistan by Amir et al and Salahuddin et al^{14, 15}. We have found a significantly (p<0.01) higher level of total homocysteine in patients with coronary artery disease as compared to control subjects.

Conclusion

This study shows that coronary artery disease is associated with mild hyperhomocysteinemia in our patients and it is not associated with other risk factors.

*Department of Biochemistry,
Services Institute of Medical Sciences,
Lahore*
theesculapio@hotmail.com
sims.edu.pk/esculapio.html

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Answer Picture Quiz

The diagnosis is acromegaly.

Acromegaly is a hormonal disorder that results when the pituitary gland produces excess growth hormone (GH). It most commonly affects middle-aged adults and can result in serious illness and premature death. Once recognized, acromegaly is treatable in most patients, but because of its slow and often insidious onset, it frequently is not diagnosed correctly.

The name acromegaly comes from the Greek words for "extremities" and "enlargement" and reflects one of its most common symptoms, the abnormal growth of the hands and feet. Soft tissue swelling of the hands and feet is often an early feature, with patients noticing a change in ring or shoe size. Gradually, bony changes alter the patient's facial features: the brow and lower jaw protrude, the nasal bone enlarges, and spacing of the teeth increases.

Overgrowth of bone and cartilage often leads to arthritis. When tissue thickens, it may trap nerves, causing carpal tunnel syndrome, characterized by numbness and weakness of the hands. Other symptoms of acromegaly include thick, coarse, oily skin; skin tags; enlarged lips, nose and tongue; deepening of the voice due to enlarged sinuses and vocal cords; snoring due to upper airway obstruction; excessive sweating and skin odor; fatigue and weakness; headaches; impaired vision; abnormalities of the menstrual cycle and sometimes breast discharge in women; and impotence in men. There may be enlargement of body organs, including the liver, spleen, kidneys and heart.

The most serious health consequences of acromegaly are diabetes mellitus, hypertension, and increased risk of cardiovascular disease. Patients with acromegaly are also at increased risk for polyps of the colon that can develop into cancer.

When GH-producing tumors occur in childhood, the disease that results is called gigantism rather than acromegaly. Fusion of the growth plates of the long bones occurs after puberty so that development of excessive GH production in adults does not result in increased height. Prolonged exposure to excess GH before fusion of the growth plates causes increased growth of the long bones and increased height.