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RELATION OF HYPERHOMOCYSTINEMIA IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Abstract:
Aim: *The aim of this study is to determine the association of hyperhomocysteinemia with acute myocardial infarction in young patients.*
Place and Duration: *We present an observational study of 12 cases of young patients with documented myocardial infarction at the Cardiology department of Bahawal Victoria Hospital, Bahawalpur for one-year duration from April 2019 to April 2020.*
Methods: *A total of 12 patients were selected for this study. Evidence of myocardial infarction was obtained by ECG, cardiac enzymes, scan or coronary angiography. Common conditions causing hyperhomocysteinemia such as kidney disease, cancer, thyroid disorders, use of antifolate medications were excluded. Hyperhomocysteinemia was classified as moderate (16-30 µmol / l), intermediate (31-100 µmol / l) and severe (> 100 µmol / l). Fasting homocysteine levels were quantified on an Axym Plus System machine (Abbott).*
Results and Conclusion: *Hence hyperhomocystinemia, a thrombotic marker which is being classified as a proximate risk factor, may act synergistically with other classical risk factors to accentuate the risk of CAD in young population. This observation needs further validation with large scale studies to justify for early screening of Homocysteine levels as it is a potentially modifiable risk factor with little economic burden.*
Key Words: *Hyperhomocysteinemia, Myocardial Infarction, atherosclerosis, thrombosis.*

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INTRODUCTION:

The relative risk of developing coronary artery disease (CAD) in the Pakistani population is highest at an early age. The pathogenesis of arterial thrombosis involves many genetic and environmental factors related to atherosclerosis and thrombosis. Well-understood genetic and environmental risk factors account for only about two-thirds of cardiovascular events, leading to an ongoing search for new markers of cardiovascular risk. In recent years, the literature on the relationship between the hemostatic system and arterial thrombosis has been growing rapidly. Studies have shown that homocysteine (Hcy), a recognized marker of thrombophilia, may be of importance in a subgroup of younger patients without conventional risk factors. However, in Pakistan there is a lack of data on the thrombophilic status of young MI patients. Homocysteine is a simple amino acid that has received much attention recently as a risk factor for atherothrombotic vascular disease. The growing interest in mild hyperhomocysteinemia as an important risk factor for cardiovascular disease arises from the observation that a rare inherited metabolic error, homocystinuria, leads to hyperhomocysteinemia, atherosclerosis, and arterial or venous thromboembolic events in early adulthood. Hyperhomocysteinemia, alone or with other thrombosis risk factors, may be associated with vascular occlusive pathology underlying a variety of clinical symptoms.

MATERIAL AND METHODS:

We present an observational study of 12 cases of young patients with documented myocardial infarction at the Cardiology department of Bahawal Victoria Hospital, Bahawalpur for one-year duration from April 2019 to April 2020. Evidence of myocardial infarction was obtained by ECG, cardiac enzymes, scan or coronary angiography. Common conditions causing hyperhomocysteinemia such as kidney disease, cancer, thyroid disorders, use of antifolate medications were excluded. Hyperhomocysteinemia was classified as moderate (16-30 µmol / l), intermediate (31-100 µmol / l) and severe (> 100 µmol / l). Fasting homocysteine levels were quantified on an Axym Plus System machine (Abbott).

RESULTS:

Of the twelve patients enrolled in this study, all had documented myocardial infarction, there were 11 men (91.6%) and 1 woman (8.3%). The mean age at MI was 32.2 years, ranging from 24 to 37 years. The analysis of CAD risk factors showed an increased level of fasting homocysteine in the range of 19-59 µmol / l (mean 31.9 µmol / l). Seven patients (58.3%) had moderate (16-30 µmol / l) and five patients (41.6%) had intermediate (31-100 µmol / l) hyperhomocysteinemia. One patient had a hypercoagulable condition (protein S deficiency) with hyperhomocysteinemia. One patient experienced a cerebrovascular accident (left MCA infarction) along with acute pre-lateral myocardial infarction. Smoking as a risk factor occurred in 6 (50%) patients, hypertension in 2 (16.6%) patients, dyslipidemia in 6 (50%) patients, 7 (58.3%) patients were overweight but none were obese, none had diabetes, and none of the patients had a positive family history of coronary artery disease. 10 out of 12 patients underwent coronary angiography; Seven (70%) patients had one-vascular CAD, 2 (20%) two-vessel CAD, and 1 (10%) patients had normal coronary arteries on coronary angiography (Table 1). The patient, who had normal coronary arteries on coronary angiography, had a history of myocardial infarction and was treated with thrombolysis. Homocysteine induces permanent damage to arterial endothelial cells, proliferation of arterial smooth muscle cells, and increases the expression / activity of key participants in vasculitis, atherosclerosis, and established plaque sensitivity. In fact, the effect of elevated homocysteine appears to be multifactorial, affecting both the structure of the vascular wall and the blood coagulation system. The proposed pathogenetic mechanisms of vascular damage are oxidative endothelial damage through suppression of the nitric oxide vasodilator, increase in the level of asymmetric dimethylarginine and Yr = year; M = male; F = female; MI = myocardial infarction; IWMI = inferior myocardial infarction; ILMI = collateral myocardial infarction; AWMI = anterior wall myocardial infarction; ASMI = pre-septal myocardial infarction; ALMI = pre-lateral myocardial infarction; NSTMI = non-ST segment elevation myocardial infarction; Hcy = homocysteine; FH = Family History; HTN = hypertension; DM = Diabetes Mellitus; LIP = lipids; BMI = body mass index; SV = single vessel; 2 V = double vessel; CAD = coronary artery disease; RCA = right coronary artery; LAD = left anterior descending artery; CIRC = Circumflex artery; LV = left ventricle.

Table - 1: General characteristics of patients

Sr. No	Age (yr)	Sex	MI	Hcy umol/L	Comorbids						Coronary Angio/Nuclear scan
					FH	HTN	DM	LIP	Smoking	BMI	
1	35	M	IWMI	20.2	-	-	-	+	+	27.54	SV-CAD (RCA)
2	35	F	ILMI	19.6	-	+	-	-	-	24.7	SV-CAD (RCA)
3	36	M	AWMI	19.46	-	-	-	+	-	22.34	2V-CAD (LAD & CIRC)
4	34	M	AWMI	40.1	-	-	-	+	+	23.3	Tc-MIBI Scan Scar antroseptal area+apex of LV
5	29	M	AWMI	22.9	-	-	-	-	-	28.37	SV-CAD (LAD)
6	29	M	ASMI	48.08	-	-	-	-	+	28.39	Normal coronaries
7	32	M	AWMI	59	-	+	-	-	-	19.48	SV-CAD (LAD)
8	24	M	ALMI	21.43	-	-	-	+	+	21.2	Not done
9	37	M	NSTMI	19	-	-	-	-	+	27.6	2V-CAD (CIRC-RCA)
10	35	M	AWMI	41.45	-	-	-	-	-	25.8	SV-CAD (LAD)
11	25	M	AWMI	>50	-	-	-	+	+	27.7	SV-CAD (LAD)
12	36	M	AWMI	21.8	-	-	-	+	-	22.9	SV-CAD (LAD)

DISCUSSION:

Experimental evidence suggests that increased homocysteine levels may induce vascular changes through several mechanisms. High levels of homocysteine induce permanent damage to arterial endothelial cells, proliferation of arterial smooth muscle cells, and increase the expression / activity of key participants in vasculitis, atherosclerosis, and established plaque sensitivity. In fact, the effect of elevated homocysteine appears to be multifactorial, affecting both the structure of the vascular wall and the blood coagulation system. Proposed pathogenetic mechanisms of vascular damage include oxidative damage to the endothelium through suppression of the nitric oxide vasodilator, increased levels of asymmetric dimethylarginine and impaired methylation, proliferation of smooth muscle blood vessels, stimulation of platelet activation and aggregation, and disturbance of normal procoagulant. - anticoagulation balance favoring thrombosis. The mean homocysteine level in Pakistani and Indian coronary artery disease patients is constant at around 19 µmol / L. This finding is significant as the South Asian population has the highest known CAD index that is common, early onset and aggressive. They are more prone to clinical events compared to other populations, even after considering all known risk factors and the degree of atherosclerosis. The mean level of homocysteine in our case series was 31.9 µmol / l, well above the standard level. Omenn et al. Provided the best estimates of the increased risk of coronary artery disease associated with elevated plasma homocysteine levels. The authors compared the relative risk between homocysteine levels above 15 µmol / L and below 10 µmol / L after adjusting for other cardiovascular risk factors and suggested that this risk difference is similar to that between serum total cholesterol levels of 7.1 and 4.9 umol. / L (275 and 189 mg / dL). In our case series, there is a positive association between hyperhomocysteinemia, smoking, and dyslipidemia. These clear interactions with conventional risk factors, especially smoking and dyslipidemia, suggest that hyperhomocysteinemia may further increase the cardiovascular risk in these patients. These observations of homocysteine and tobacco smoking could have a severe impact on the high-smoking population of Pakistan. Therefore, hyperhomocystinemia, a thrombotic marker that is classified as a proximal risk factor, may synergize with other classical risk factors, enhancing the risk of CAD in a young population. This observation needs

further validation in large-scale studies to warrant an early screening of homocysteine levels as it is a potentially modifiable risk factor with low economic burden.

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