International Journal of Advanced Community Medicine

E-ISSN: 2616-3594
P-ISSN: 2616-3586
www.comedjournal.com
IJACM 2022; 5(3): 11-13
Received: 10-05-2022
Accepted: 16-06-2022

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Assessment of role of homocysteine in coronary heart disease

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DOI: https://doi.org/10.33545/comed.2022.v5.i3a.242

Abstract
Background: Homocysteine has been under a lot of speculation since its discovery in 1932. The present study was conducted to assess the role of homocysteine in coronary heart disease.
Materials and methods: 76 patients of coronary heart disease of both genders were included. The body mass index was calculated as weight (kg)/height (m)2. Blood pressures were measured. Serum total homocysteine was measured. Serum total and HDL cholesterol were determined with standard methods. Serum creatinine was determined with a modified Jaffe´ method.
Results: Out of 76 patients, males were 52 and females were 24. The mean BMI (Kg/m2) was 25.4, SBP (mm Hg) was 154.2, DBP (mm Hg) was 86.4, serum cholesterol (mmol/L) was 6.52, serum HDL (mmol/L) was 1.08, serum creatinine (µmmol/L) was 112.9. Co-morbidities comprise of hypertension in 34, diabetes mellitus in 8, myocardial infarction in 14, stroke in 7 and smoking in 26. The difference was significant ($P< 0.05$). Crude value was 1.09 and adjusted value was 1.56 in CHD and crude value was 1.88, adjusted value was 1.27, normotensive adjusted value was 6.17 and hypertensive adjusted value was 1.64.
Conclusion: A high homocysteine level is common and is strongly associated with the prevalence of coronary heart disease and cerebrovascular disease.

Keywords: Cardiovascular diseases, Homocysteine, cholesterol

Introduction
Homocysteine has been under a lot of speculation since its discovery in 1932. Its chemical properties showed a similarity to cysteine, hence the name homocysteine. The heating of the amino acid methionine with sulphuric acid led to this amino acid of interest. The importance of this discovery cannot be emphasized on without alluding to the 1955 Nobel Prize in Chemistry, awarded to Vincent du Vigneaud "For his work on biochemically important sulphur compounds, especially for the first synthesis of a polypeptide hormone" [1].
Cardiovascular diseases (CVD) as the name suggests, comprises diseases of the heart and blood vessels [2]. Cardiovascular disease is believed to account for one third of all deaths worldwide, and the prevalence is still on the rise. CVD is among the diseases with multiple contributing factors, hence making it difficult to pinpoint a particular factor alone. The main factor that is of relevance to this study is homocysteine. Coronary artery disease is the narrowing or blockage of the arteries and vessels that supply oxygen and nutrients to the heart [3]. The severity of coronary artery disease is classified as single vessel, double vessels and triple vessels disease using the Gensini scoring system [4]. Homocysteine has been recognized as a risk factor as early as 1990s, for the presence of atherosclerotic vascular disease and hypercoagulability states. Subgroup analyses conducted in a study also showed that elevated homocysteine was associated with higher risk of coronary artery disease in patients with chronic renal dysfunction [5]. The present study was conducted to assess the role of homocysteine in coronary heart disease.

Materials and Methods
The present study comprised 76 patients of coronary heart disease of both genders. The

consent was obtained from all enrolled patients. The diagnosis of myocardial infarction required 2 or more of the following 3 criteria: severe chest pain lasting for 20 minutes that did not disappear in rest, characteristic changes on electrocardiography, and specific enzyme elevations.
Data such as name, age, gender etc. was recorded. The body mass index was calculated as weight (kg)/height (m) 2. Blood pressures were measured. Hypertension was defined as a systolic blood pressure of >160 mm Hg, a diastolic blood pressure of >95 mm Hg, and/or use of antihypertensive drugs. Venous blood samples were obtained in the non-fasting state. Serum total homocysteine was measured. Serum total and HDL cholesterol were determined with standard methods. Serum creatinine was determined with a modified Jaffe´ method. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table 1: Distribution of patients

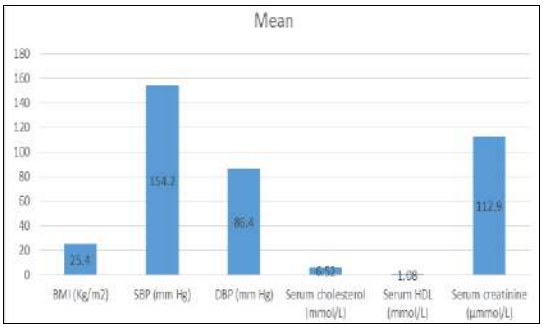
Total: 76		
Gender	**Males**	**Females**
Number	52	24

Table 1 shows that out of 76 patients, males were 52 and females were 24.

Table 2: Assessment of parameters

Parameters	Mean
BMI (Kg/m^2)	25.4
SBP (mm Hg)	154.2
DBP (mm Hg)	86.4
Serum cholesterol (mmol/L)	6.52
Serum HDL (mmol/L)	1.08
Serum creatinine (µmmol/L)	112.9

Table 2, graph 1 shows that mean BMI (Kg/m2) was 25.4, SBP (mm Hg) was 154.2, DBP (mm Hg) was 86.4, serum cholesterol (mmol/L) was 6.52, serum HDL (mmol/L) was 1.08, serum creatinine (µmmol/L) was 112.9.

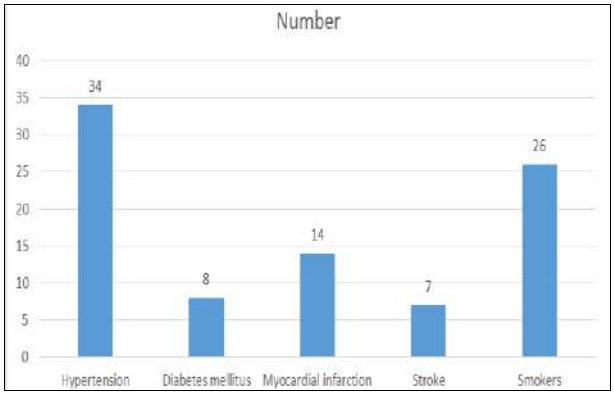


Graph 1: Assessment of parameters

Table 3: Co- morbidities

Co- morbidities	Number	P value
Hypertension	34	0.02
Diabetes mellitus	8	
Myocardial infarction	14	
Stroke	7	
Smokers	26	

Table 3, graph 2 shows that co- morbidities comprise of hypertension in 34, diabetes mellitus in 8, myocardial infarction in 14, stroke in 7 and smoking in 26. The difference was significant (P< 0.05).



Graph 2: Co- morbidities

Table 4: Relative risks and 95% CIs for mortality from coronary heart disease and cerebrovascular disease

Mortality	Variables	Value
CHD	Crude	1.90
	adjusted	1.56
CVDs	Crude	1.88
	adjusted	1.27
	Normotensive adjusted	6.17
	Hypertensive adjusted	1.64

Table 4 shows that crude value was 1.09 and adjusted value was 1.56 in CHD and crude value was 1.88, adjusted value was 1.27, normotensive adjusted value was 6.17 and hypertensive adjusted value was 1.64.

Discussion

Hyperhomocysteinemia is an independent risk factor for atherosclerotic disease in the middle-aged [6]. The associations between homocysteine and coronary heart and cerebrovascular disease are not consistent [7]. One possibility is that homocysteine is related to other cardiovascular risk factors, ie, that homocysteine is not an independent cause of vascular disease, and that studies showing an association of hyperhomocysteinemia and cardiovascular risk have not been fully adjusted for possible confounders [8]. However, plausible biological mechanisms have been demonstrated by which high homocysteine levels may lead to vascular disease: homocysteine is thought to induce endothelial dysfunction with respect to the regulation of vasomotor tone and hemostatic balance and to stimulate vascular smooth muscle cell proliferation, both important events in the pathogenesis of atherothrombotic disease [9]. Moreover, severe hyperhomocysteinemia in young people is strongly associated with arteriosclerosis and arterial and venous thrombosis at a young age [10]. These findings constitute important evidence in favor of a causal association between homocysteine and vascular disease [11]. The present study was conducted to assess role of homocysteine in coronary heart disease.
We found that out of 76 patients, males were 52 and females were 24. Stehouver *et al.* [12] investigated whether a high serum homocysteine level is a risk factor for vascular disease in 878 elderly men (mean age at baseline, 71.5 years; range, 64 to 84 years) in a population-based, representative cohort. Thirty-one percent had non-fasting homocysteine levels of $17 mmol/L. After adjustment for other major risk factors, high homocysteine levels at baseline (the third compared with the first tertile) were associated with an increased baseline prevalence of myocardial infarction (odds ratio [OR], 1.81; 95% confidence interval [CI], 1.07 to 3.08; P for trend, 0.03) and with a marginally significant increase in the risk of dying of

coronary heart disease (relative risk [RR], 1.58; 95% CI, 0.93 to 2.69; P for trend, 0.09) but not with an increased risk of first-ever myocardial infarction. In addition, high homocysteine levels at baseline were associated with an increased baseline prevalence of stroke (OR, 4.61; 95% CI, 1.79 to 11.89; P for trend, 0.002) and with an increased risk of dying of cerebrovascular disease in subjects without hypertension (RR, 6.18; 95% CI, 2.28 to 16.76) but not in those with hypertension. High homocysteine levels were associated with an increased risk of first-ever stroke among normotensive subjects that was not statistically significant (RR, 1.77 [95% CI, 0.83 to 3.75; P for trend, 0.14])

In our study the mean BMI (Kg/m2) was 25.4, SBP (mm Hg) was 154.2, DBP (mm Hg) was 86.4, serum cholesterol (mmol/L) was 6.52, serum HDL (mmol/L) was 1.08, serum creatinine (µmmol/L) was 112.9. We found that comorbidities include hypertension in 34, diabetes mellitus in 8, myocardial infarction in 14, stroke in 7 and smoking in 26. We observed that crude value was 1.09 and adjusted value was 1.56 in CHD and crude value was 1.88, adjusted value was 1.27, normotensive adjusted value was 6.17 and hypertensive adjusted value was 1.64. Research has indicated a relationship between moderately elevated homocysteine levels and the risk of CVD (coronary, heart, cerebrovascular and peripheral artery diseases). The homozygous mutation of C,S can cause severe hyperhomocysteinemia where homocysteine concentration is up to 40-fold of the normal levels. This disease occurs in approximately 1 of 100,000 live births. When untreated, a vascular event (stroke, myocardial infarction, other thromboembolic complication) occurs in about half of these patients before the age of 30. Another cause of rare, genetically mediated severe hyperhomocysteinemia is due to homozygous mutations of MTHFR. People with these mutations have been noted to have premature cardiovascular diseases. But a large meta-analysis showed the lack of statistically significant association between MTHFR mutations and coronary heart disease except in Middle East and Japan, where it portrayed statistical significance [13].

Conclusion

Authors found that a high homocysteine level is common and is strongly associated with the prevalence of coronary heart disease and cerebrovascular disease.

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