

Association of Serum Homocysteine and Coronary Heart Disease in North Indian Population

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Abstract—Elevated serum homocysteine levels are associated with an increased risk of coronary heart disease (CHD). In spite of several studies, hyperhomocysteinemia has not been accepted yet as an established cardiovascular risk factor and which remains controversial. Therefore, we aimed to estimate the association between hyperhomocysteinemia and CHD and to determine the role of homocysteine as a risk factor for CHD. This study was designed to investigate the association between CHD and hyperhomocysteinemia in northern population. In this cross-sectional study, 100 residents (26 male and 74 female) of Bathinda region, aged 20-70 years old were assessed for ischemic heart disease (CHD), resting electrocardiographic (ECG) and CHD risk factor (serum homocysteine) were compared with 100 matched age and sex controls. Mean plasma total homocysteine (tHcy) in men was significantly higher than in women ($P = 0.05$). There was significant difference in mean serum vitamin B12, homocysteine and folate between the ischemic and non-ischemic individuals ($P < 0.05$, 0.05 and 0.05 respectively). According to the results, high serum level of tHcy by itself is a CHD risk factor in coronary heart disease, and it should be considered for reduction in CHD patients.

Keywords: Homocysteine, Coronary heart disease and Electrocardiography.

Introduction

Homocysteine (Hcys) is an essential amino acid. It has been known as a novel and independent risk factor for coronary heart disease (CHD) [1,4]. The prevalence of hyperhomocysteinemia varies between 5% and 30% in the general population [5]. In India, the burden of cardiovascular disorders, especially CHD, is high, and these are the leading cause of mortality. Genetic factors, smoking, hypertension, serum creatinine, total cholesterol and protein and nutritional factors such as vitamin B6,

B12 and folate deficiency determine serum total homocysteine (tHcy) concentrations [2]. It has been shown that elevated serum Hcys levels are associated with an increased risk of ischemic heart disease (IHD) and stroke [3,7,8]. Also, higher Hcys concentrations in IHD or stroke patients than in controls has been reported [3,9,10]. Some prospective and case-control studies with inconsistent results, some with highly significant

results [10,11] and others with no association have been observed [4,12,13]. A recent study has indicated that increase in homocysteine and other novel risk factors have been associated with an increase in Framingham risk score in elderly people [14]. In spite of several studies, hyperhomocysteinemia has not been accepted yet as an established cardiovascular risk factor and remains controversial. Therefore, we aimed to investigate the association between homocysteine and IHD and to determine the role of homocysteine as a risk factor for IHD.

Materials and Methods

The study was carried out in the duration November, 2017 – November, 2018. This study included 100 consecutive newly diagnosed patients, 100 age matched controls. The study was done after approval from the institutional ethics committee. An informed consent was being taken from the patients prior to inclusion in the study. Inclusion Cases were selected among patients admitted to the Cardiac Care unit, Adesh Institute of Medical Sciences and Research. With symptoms of acute myocardial infarction with or without electrocardiographic signs of elevated ST segment. Controls were subjects treated in the outpatient clinic of the Hospital, who had no cardiovascular disease or other chronic diseases such as renal failure.

Laboratory assays - Venous blood samples from the cases were obtained at baseline from eight to twelve hours after symptom presentation and Plasma was immediately obtained by centrifugation at 4°C, for 15 minutes at 3000 rpm. Aliquots of plasma were stored for batch analysis at -20°C within 1 hour of sampling. In the controls, samples were obtained after an overnight 12-hour fast. Plasma tHcy Homocysteine levels Folate and vitamin B12 (Vit B12) were measured simultaneously assayed by Biosystem Fully Automated A-15 (BIOSYSTEM). All the research was carried out in Central Laboratory of Adesh Institute of Medical Sciences and Research, Bathinda. We defined hyperhomocysteinemia (Hcys) as Hcys > 15 mmol/L. 1 Serum folate levels < 11 nmol/L and vitamin B12 concentration < 185 pmol/L considered as

vitamin deficiency. A twelve-lead electro-cardiogram (ECG) was obtained from all participants in the resting position.

Statistical Analysis

For interpretation of data SPSS software was used. The demographic parameters of cases and controls were compared by Chi-squared analysis. Independent t-test was used to find if levels of Hcys, Folic Acid and Vitamin B12 differ significantly in cases and controls. The results were shown as mean \pm SD, and $P < 0.05$ was considered significant.

Ethical Considerations

The study was revised and approved by the Institutional Research Committee and Ethics Committee of the Adesh Institute of Medical Sciences and Research University, Bathinda. Informed consent was signed by the subjects who agreed to participate in the study.

Results

The demographic information of cases and controls which includes sex, age, area, and BMI are shown in Table-1. The mean levels of homocysteine, folic acid and vitamin B12 in cases and controls are shown in Table 2. Homocysteine levels in controls were within normal limits ($8.7 \mu\text{mol/l} \pm 3.1$) but were higher in cases ($13.8 \mu\text{mol/l} \pm 6.1$).

Variable		Cases N=100		Controls N=100		X ²
		n	%	n	%	
Sex	Male	42	42	39	39	0.885
	Female	58	58	61	61	
Age	30-40	20	20	21	21	0.655
	41-50	24	24	28	28	
	51-60	56	56	51	51	
Area	Rural	59	59	55	55	0.938
	Urban	41	41	45	45	
BMI	18.5 to 24.9	20	20	44	44	0.053
	25.0 to 29.9	53	53	22	22	
	30.0 and above	27	27	5	5	

Folic acid levels in cases were 9.4 ± 3.6 and 14.0 ± 4.5 in controls. Vitamin B12 in cases were 201.4 ± 156.7 and 300 ± 180.4 in controls. The differences in mean homocysteine, Folic Acid and Vit B12 levels between cases and controls were statistically significant ($p < 0.05$). There was significant relationship between hyperhomocysteinemia, Vit B12 deficiency and folate deficiency with ischemic and non-ischemic group. There was significant correlation between Hcys, Folic Acid and Vit B12 levels in CHD patients.

	Cases	Control	p-value
Hcys	13.8 ± 6.1	8.7 ± 3.1	< 0.05
Folic Acid	9.4 ± 3.6	14.1 ± 4.5	< 0.05
Vit B 12	201.4 ± 156.7	300 ± 180.4	< 0.05

Discussion

This study investigated the association between hyperhomocysteinemia and CHD. Significant relationship was found between serum tHcy levels and CHD according to the ECG findings. Many studies have shown association between plasma tHcy concentrations and CHD. They have reported elevated plasma tHcy as an independent risk factor for CHD [3,4,25,26]. These findings were supported by the results of a meta-analysis which indicated that tHcy is a modest predictor of CHD and stroke risk in a healthy population independent of traditional cardiovascular risk factors [27]. Nygard et al. study could only show a weak relationship between Hcy and angiographic findings [4], while other studies revealed a positive association between plasma tHcy and risk of severe coronary atherosclerosis according to angiography results [28]. Our findings disagree with Nikkari et al who did not find significant difference in serum tHcy between men with angina pectoris and controls [29] Nikkari et al. observed higher serum tHcy in men with previous myocardial infarction than in controls results which have been repeated in several previous studies [5, 10, 29]. In the present study, tHcy in men was higher than in women in the study population and it was elevated in the people with ischemic heart disease. Retterstol et al., investigated a cohort of young CHD patients, dissimilar to our findings could not see association between serum tHcy and CHD. They showed that tHcy was only a predictor of total and cardiac mortality in older ages [23]. Although in the present study tHcy levels increased by age, in one report from (India), it was higher in younger-age subjects [26]. One of these studies showed that administration of folic acid, vitamin B6, and vitamin B12 for 5 years reduce the incidence of major vascular events in high-risk patients with vascular disease (including cardiovascular causes and myocardial infarction) [30,31]. These are two limitations of the present study. So, Up to now, different surveys have reported various results. However, future cohort and case-controlled studies with larger sample size are required to confirm these results in this region.

Conclusion

According to the results, high serum level of tHcy by itself is a CHD risk factor in coronary heart disease, it has been suggested that tHcy is an independent predictor of mortality in stable and acute CHD and it should be considered for reduction in CHD patients.

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