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Original Research Article

An Observational Study to Investigate the Association of Homocystine Level and Lipid Profiles with Ischemic Heart Disease

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Abstract:

Aim: The aim of the present study was to investigate the association of homocystine level and lipid profiles with ischemic heart disease.

Methods: This prospective case control study was conducted at Department of Cardiology over a period of one year. Patients of Ischemic Heart Disease (IHD) admitted in Department of Cardiology were included. The data for the study was collected from the inpatients and outpatients of the hospital, who fulfilled the inclusion and exclusion criteria. Normal healthy population was selected from people who came for routine health checkup and staff members of the hospital.

Results: There was a significant difference between homocysteine levels of cases and controls. Thus we found that higher homocysteine levels were significantly associated with IHD in our study. By using chi-square test p-value >0.05, there was no significant difference between cholesterol levels among the cases and controls. Thus we did not find a strong association between hypercholesterolemia and IHD. There was no significant difference between triglyceride levels among the cases and controls. There was no significant difference between HDL levels among the cases and controls.

Conclusion: Based on the outcome of the present study we conclude that Hyperhomocysteinemia status is independently associated with hypertriglyceridemia, high total cholesterol level, high LDL level and low HDL levels in the blood.

Keywords: Ischemic heart disease, homocysteine, cholesterol, triglyceride.

Introduction

Hyperhomocysteinemia (HHcy) has been regarded as a new modifiable risk factor for cardiovascular disease (CVD) through various mechanisms, including vascular endothelium damage, stimulation of smooth muscle cell proliferation, enhanced low-density lipoprotein cholesterol (LDL-C) peroxidation and thrombosis activation.[1,2] Previous studies also established that there was a possible link among HHcy, dyslipidemia and atherosclerosis. Regarding Hcy, an inverse association between this amino acid and lipoproteins, especially high-density lipoprotein cholesterol (HDL-C), has been well described in humans and various animal models of HHcy.[3] HHcy might also increase the risk of CVD in dyslipidemia patients.[4-6]

Although the mechanism of the link is not thoroughly known, recent studies strongly demonstrated the importance of the metabolic balance between S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), phosphatidylcholine (PC), phosphatidylethanolamine (PE) and choline in Hcy metabolism, hypolipoproteinemia, liver function, and CVD.[3,7] Several studies relating HHcy to disturbed HDL-C metabolism showed that Hcy can reduce circulating HDL-C via inhibiting ApoA-I protein synthesis and enhance HDL-C clearance.[8,9]

Ischemic heart disease (IHD) is a major public health problem in India. Its mortality and disability rises very rapidly with age. It occurs at an early age of life. This cannot be explained by the conventional risk factors like hyperlipidemia, smoking, diabetes mellitus, hypertension, abdominal obesity, stress, physical inactivity, insulin resistance. The discovery of homocysteine (Hcy) as a risk factor in vascular diseases diverted the attention of medical practitioners and researchers from conventional risk

factors.[10] It is now well established that elevated circulating level of Hcy is associated with IHD.[11,12] The severe hyperhomocysteinemia is seen in 5 - 7 % of general population who do not show clinical signs and symptoms of IHD in their early life.[13]

Association between HHcy, dyslipidemia and atherosclerosis has already been studied extensively.[14] An inverse association between HHcy and HDL-C has been found in humans in various studies.[15] Recent studies have strongly showed the importance of metabolic balance between homocysteine metabolism, hypolipoproteinemia, liver function and cardiovascular disease.[16,17]

The aim of the present study was to investigate the association of homocystine level and lipid profiles with ischemic heart disease.

Materials and Methods

This prospective case control study was conducted at Department of Cardiology, Narayan Medical College and Hospital, Sasaram, Rohtas, Bihar, India over a period of one year . Patients of Ischemic Heart Disease (IHD) admitted in Department of Cardiology were included. The data for the study was collected from the inpatients and outpatients of the hospital, who fulfilled the inclusion and exclusion criteria. Normal healthy population was selected from people who came for routine health checkup and staff members of the hospital.

All included individuals were grouped into cases and controls as follows:

Group I (Cases): 50 cases of ischemic Heart disease
Group II (Controls): 50 normal healthy people
Inclusion criteria (Group I-cases).

50 randomly selected patients who came to OPD / IPD of our hospital and diagnosed as Ischemic Heart Disease.

Exclusion criteria (Group I-cases)

- Patients < 12 years
- Patients on Haemodialysis
- Patients with renal transplant
- Patients on drugs such as methotrexate, theophylline, metformin and niacin
- Patients with other renal, liver or major systemic disorder.

Inclusion criteria (Group II-controls)

- Lab staff of our hospital
- People who came for routine health check-up in our hospital
- Resident doctors and consultants of our hospital

Exclusion criteria (Group II-controls)

- DM/HTN
- vitamin supplement
- Any apparent disease

After obtaining informed consent they were evaluated through a structured proforma designed especially for this study. For every patient detailed history including personal and family history were taken. Each patient was subjected to thorough general examination and systemic examination. The lab investigations done in each patient were Serum B12, Homocysteine, Lipid profile and fasting (F) and postprandial (PP) blood sugar level (BSL).

Definitions

1. Patients having BP >140/90 on 2 occasions and those who were already on antihypertensive medication were considered to be hypertensive.
2. Homocysteine levels </=15µmol/l were considered normal and >15µmol/l were considered high.
3. Normal values of - i. cholesterol <200mg/dl; ii. TG <150 mg/dl; iii. HDL <40mg/dl in males and
4. <50mg/dl in females; iv. LDL < 100mg/dl.
5. Patients with Fasting BSL>126mg/dl and Postprandial BSL>200mg/dl and those who were already on anti-diabetic treatment were considered diabetic.
6. People who consumed non-vegetarian diet at least thrice a week were considered non- vegetarians.

Homocysteine estimation

Homocysteine assay is a one-step immunoassay for the quantitative determination of total L-homocysteine in human serum or plasma using Chemiluminescent Microparticle Immunoassay (CIMA) technology, with flexible assay protocols, referred to as Chemiflex. It was estimated by using Architect i1000 Sr instrument.

Lipid profile estimation

Cholesterol, HDL, Triglycerides were measured enzymatically using specific reagents. Vitros 5.1 FS, dry chemistry was used for estimation of lipid profile.

Statistical analysis

SPSS for windows (version 21.0, SPSS Inc., Chicago, IL, USA) was employed for data analysis. $P < 0.05$ was considered as significant. Fisher's exact test was used to determine if there are nonrandom associations between two categorical variables

Results

Table 1: Distribution of patients with respect to homocysteine in group 1 and 2

Homocysteine	Groups		P Value
level	Group 1 (cases)	Group 2 (controls)	
≤ 15	12 (24%)	24 (48%)	< 0.001
> 15	38 (76%)	26 (52%)	
Total	**100**	**100**	

There was a significant difference between homocysteine levels of cases and controls. Thus we found that higher homocysteine levels were significantly associated with IHD in our study.

Table 2: Distribution of patients with respect to cholesterol in group 1 and group 2

Cholesterol level	Groups		P Value
	Group 1 (cases)	Group 2 (controls)	
< 200	38 (76%)	35 (70%)	0.890
≥ 200	12 (24%)	15 (30%)	
Total	**100**	**100**	

By using chi-square test p-value >0.05, there was no significant difference between cholesterol levels among the cases and controls. Thus we did not find a strong association between hypercholesterolemia and IHD.

Table 3: Distribution of patients with respect to triglycerides in Group 1 and Group 2

Triglycerides Level	Groups		P Value
	Group 1 (cases)	Group 2 (controls)	
< 150	35 (70%)	33 (66%)	0.999
≥ 150	15 (30%)	17 (34%)	
Total	**100**	**100**	

There was no significant difference between triglyceride levels among the cases and controls.

Table 4: Distribution of patients with respect to HDL in Group 1 and Group 2

HDL Level	Groups		P Value
	Group 1 (cases)	Group 2 (controls)	
< 150	40 (80%)	34 (68%)	0.960
≥ 150	10 (20%)	16 (32%)	
Total	**100**	**100**	

There was no significant difference between HDL levels among the cases and controls.

Discussion

The discovery of homocysteine as a risk factor in vascular diseases diverted the attention of medical practitioners and researchers from conventional risk factors.[18] There are studies which have shown correlation between elevated homocysteine as the risk factor for atherosclerotic vascular disease.[19] During the last 15 years it has been thoroughly documented that also moderately elevated homocysteine levels in serum or plasma is a strong and independent risk factor for occlusive arterial disease, and of venous thrombosis.[20,21] Homocysteine (Hcy) is considered to be associated with hyperlipidaemia. An understanding of its metabolism and factors that effect its regulation will help in the development of therapeutic strategies which may eventually lower the risk of atherosclerosis in humans. Possible mechanisms of atherosclerosis due to hyperhomocysteinemia (HHcy) include damage to inner vascular membrane, augmentation of smooth muscle cell proliferation, increase low–density lipoprotein cholesterol peroxidation and activation of thrombos formation.[22,23]

There was a significant difference between homocysteine levels of cases and controls. Thus we found that higher homocysteine levels were significantly associated with IHD in our study. By using chi-square test p-value >0.05, there was no significant difference between cholesterol levels among the cases and controls. Thus we did not find a strong association between hypercholesterolemia and IHD. There was no significant difference between triglyceride levels among the cases and controls. There was no significant difference between HDL levels among the cases and controls. These findings were similar to the study of Wasilewska et al.[24] Mahalle N et al[25] studied 300 Indian subjects with proven coronary heart disease. Homocysteine was found to be positively associated with TG and VLDL-C, and negatively with HDL-C in their study. Yadav reported that there was no significant correlation between plasma homocysteine and TC, HDL- C, and TG in 60 ischemic heart disease patients. A study by de Luis DA et al[26] that enrolled 155 diabetes patients and found no significant association between homocysteine and lipids either.

The interaction between hyperlipidaemia and Hcy metabolism has been extensively studied.[27,28] It has been found that methionine can alter cholesterol metabolism and there is a weak positive correlation between circulating homocysteine and plasma cholesterol.[25] However, the relationship between HHcy and hyperlipidaemia have not been conclusively proved up til now.[29] It has been postulated that the low ratio between phosphatidylcholine (PC) and phosphatidylethanolamine (PE) caused by HHcy is a major factor for triglycerides accumulation. Hcy enhances the augments the expression of sterol regulatory element-binding proteins which leads to increased intracellular accumulation of TC and TG.[30] Hcy also leads to protein misfolding in the endoplasmic reticulum which affects lipoprotein particle production in the cell.[31] DNA hypomethylation has been postulated to be the mechanism which suggests that Hcy leads to lipid disorders and atherosclerosis in blood vessels.[32]

Conclusion

Based on the outcome of the present study we conclude that Hyperhomocysteinemia status is independently associated with hypertriglyceridemia, high total cholesterol level, high LDL level and low HDL levels in the blood.

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