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An Observational Study Determining the Correlation of Homocysteine and Lipid Profile Parameters with Ischemic Heart Disease

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ABSTRACT

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

Methods: This 12-month prospective case control study was undertaken at a tertiary care hospital. The Department of Medicine accepted IHD patients. The research gathered data from hospital inpatients and outpatients who met inclusion and exclusion criteria. Healthy persons were picked among hospital workers and regular checkup patients.

Results: The homocysteine levels of the patients and controls differed significantly. As a result, we discovered that in our investigation, increased homocysteine levels were substantially linked to IHD. The chi-square test revealed no significant difference in cholesterol levels between the patients and controls (p-value >0.05). As a result, there was no evidence of a substantial link between hypercholesterolemia and IHD. Triglyceride levels did not significantly vary between the patients and controls. HDL levels did not significantly vary between the patients and controls.

Conclusion: According to this research, hyperhomocysteinemia is independently linked to hypertriglyceridemia, high total cholesterol, high LDL, and low HDL values.

Keywords: Ischemic heart disease, homocysteine, cholesterol, triglyceride

1. INTRODUCTION

The discovery of homocysteine as a risk factor in vascular diseases diverted the attention of medical practitioners and researchers from conventional risk factors.[1] There are studies which have shown correlation between elevated homocysteine as the risk factor for atherosclerotic vascular disease.[2] 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.[3-4] As many as 50% of patients with stroke, and other atherothrombotic disease have high homocysteine levels (over 15µmol/L). [5] An inverse association between homocystine and lipoproteins, especially high-density lipoprotein cholesterol, has been well described in humans and various animal models of hyperhomocystinemia.[6]

Coronary artery disease (CAD) is the leading cause of death worldwide and remains a major

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health problem in both developed and developing countries.[7] Traditional lipid parameters, such as increased serum levels of total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and apolipoprotein (Apo) B or low levels of high-density lipoprotein cholesterol (HDL-C) and ApoAI, are among the most important modifiable risk factors for CAD.[8-9] Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of death worldwide, thus early prevention and treatment are extremely important. In addition to obesity, hyperglycemia, hypertension, and dyslipidemia, it has been confirmed that homocysteine (Hcy) is an emerging and independent risk factor for cardiovascular diseases, including ischemic heart disease, stroke, and peripheral vascular disease.[10-11]

The meta-analysis suggested that patients with heart failure and ischemic stroke had significantly elevated plasma Hcy levels compared with normal controls.[12-13] It was estimated by Boushey et al. that approximately 10% of coronary artery disease might be attributed to hyperhomocysteinemia (HHcy).[14] Inversely, B vitamins supplementation, a therapy to lower plasma Hcy levels, appeared to decrease cardiovascular events in subjects with normal renal function.[15] The mechanism linking HHcy to the risk of ASCVD is still unclear. Hcy is a type of thiol-containing amino acid and is one of the critical intermediates of the methionine cycle and cysteine metabolism.[16] Previous epidemiological studies and animal experiments implicated that inflammation reaction, oxidative stress, endothelial dysfunction, endoplasmic reticulum (ER) stress, and epigenetic control of gene expression were all potential mediators of HHcy-induced ASCVD.[17-19]

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

2. MATERIALS AND METHODS

This 12-month prospective case control study was undertaken at a tertiary care hospital. The Department of Medicine accepted IHD patients. The research gathered data from hospital inpatients and outpatients who met inclusion and exclusion criteria. Healthy persons were picked among hospital workers and regular checkup patients.

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

Group I (Cases): 100 cases of ischemic Heart disease Group II (Controls): 100 normal healthy people

Inclusion criteria (Group I-cases)

- 100 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

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- Any apparent disease

After informed consent, patients were examined using a study-specific proforma. Every patient had a personal and family history taken. Each patient had a complete general and systemic assessment. Each patient's lab tests included serum B12, homocysteine, lipid profile, and fasting and postprandial blood sugar.

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.

3. RESULTS

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

Homocysteine level	Groups		P Value
	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%)	>0.05
≥ 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%)	>0.05
≥ 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

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	Group 1 (cases)	Group 2 (controls)	
< 150	40 (80%)	34 (68%)	>0.05
≥ 150	10 (20%)	16 (32%)	
Total	**100**	**100**	

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

4. DISCUSSION

Homocysteine (Hcy) is believed to be linked to hyperlipidemia. Comprehending the metabolism of atherosclerosis and the variables that impact its control would aid in the formulation of treatment approaches that might potentially reduce the likelihood of atherosclerosis in people. Possible causes of atherosclerosis caused by hyperhomocysteinemia (HHcy) include the following: injury to the inner arterial membrane, enhancement of smooth muscle cell proliferation, elevation of low-density lipoprotein cholesterol peroxidation, and initiation of thrombus formation.[20,21]

There was a notable disparity in the homocysteine levels between the patients and controls. Our investigation revealed a substantial correlation between elevated homocysteine levels and IHD. Based on the chi-square test with a p-value greater than 0.05, there was no statistically significant difference seen in cholesterol levels between the cases and controls. Therefore, we did not discover a significant correlation between hypercholesterolemia and ischemic heart disease (IHD). There was no discernible disparity in triglyceride levels between the patients and controls. There was no substantial disparity in HDL values between the patients and controls. These results were consistent with the research conducted among 300 Indian individuals who had confirmed coronary heart disease. The research revealed a positive correlation between homocysteine and TG and VLDL-C, as well as a negative correlation with HDL-C. Yadav observed that there was no notable association between plasma homocysteine levels and TC, HDL-C, and TG in a group of 60 patients with ischemic heart disease.[22,23] Research conducted by de Luis DA et al[24], which included 155 individuals with diabetes, found no significant correlation between homocysteine and lipids.

The relationship between hyperlipidaemia and Hcy metabolism has been well investigated.[25,26] Research has shown that methionine has the ability to modify cholesterol metabolism. Additionally, there exists a little positive relationship between the levels of circulating homocysteine and plasma cholesterol.[23] Nevertheless, the association between HHcy and hyperlipidemia has not been definitively shown so far.[27] HHcy has been hypothesized to be a significant contributor to the buildup of triglycerides because to the decreased ratio of phosphatidylcholine (PC) to phosphatidylethanolamine (PE). Hcy amplifies the expression of sterol regulatory element-binding proteins, resulting in heightened intracellular buildup of TC and TG.[28] Hcy also induces protein misfolding in the endoplasmic reticulum, hence impacting the synthesis of lipoprotein particles inside the cell.[29] The mechanism by which Hcy contributes to lipid problems and atherosclerosis in blood vessels is believed to include DNA hypomethylation.[30]

5. CONCLUSION

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As a result of the findings of the current research, we have come to the conclusion that the presence of hyperhomocysteinemia is independently linked to hypertriglyceridemia, high total cholesterol levels, high LDL levels, and low HDL levels in the blood.

6. REFERENCES

1. Yadav AS, Bhagwat VR, Rathod IM. Relationship of plasma homocysteine with lipid profile parameters in ischemic heart disease. Indian journal of clinical Biochemistry. 2006 Mar;21:106-10.
2. Narang AP, Verma I, Kaur S, Narang A, Gupta S, Avasthi G. Homocysteine--risk factor for ischemic stroke. Indian J Physiol Pharmacol. 2009 Jan 1;53(1):34-8.
3. Ueland PM. Homocysteine species as components of plasma redox thiol status. Clinical chemistry. 1995 Mar 1;41(3):340-2.
4. Still RA, McDowell IF. ACP Broadsheet No 152: March 1998. Clinical implications of plasma homocysteine measurement in cardiovascular disease. Journal of clinical pathology. 1998 Mar 1;51(3):183-8.
5. Malinow MR, Bostom AG, Krauss RM. Homocyst (e) ine, diet, and cardiovascular diseases: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. Circulation. 1999 Jan 12;99(1):178-82.
6. Obeid R, Herrmann W. Homocysteine and lipids: S-adenosyl methionine as a key intermediate. FEBS letters. 2009 Apr 17;583(8):1215-25.
7. Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. The Lancet. 2007 Dec 8;370(9603):1929-38.
8. Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S, Kannel WB. Incidence of coronary heart disease and lipoprotein cholesterol levels: the Framingham Study. Jama. 1986 Nov 28;256(20):2835-8.
9. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs Jr DR, Bangdiwala S, Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation. 1989 Jan;79(1):8-15.
10. de Oliveira Leite L, Costa Dias Pitangueira J, Ferreira Damascena N, Ribas de Farias Costa P. Homocysteine levels and cardiovascular risk factors in children and adolescents: systematic review and meta-analysis. Nutrition Reviews. 2021 Sep 1;79(9):1067-78.
11. Yuan S, Mason AM, Carter P, Burgess S, Larsson SC. Homocysteine, B vitamins, and cardiovascular disease: a Mendelian randomization study. BMC medicine. 2021 Dec;19:1-9.
12. Zhang T, Jiang Y, Zhang S, Tie T, Cheng Y, Su X, Man Z, Hou J, Sun L, Tian M, Zhang Y. The association between homocysteine and ischemic stroke subtypes in Chinese: a meta-analysis. Medicine. 2020 Mar 1;99(12):e19467.
13. Jin N, Huang L, Hong J, Zhao X, Chen Y, Hu J, Cong X, Xie Y, Pu J. Elevated homocysteine levels in patients with heart failure: A systematic review and meta-analysis. Medicine. 2021 Aug 20;100(33):e26875.
14. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: probable benefits of increasing folic acid intakes. Jama. 1995 Oct 4;274(13):1049-57.

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15. Spence JD, Yi Q, Hankey GJ. B vitamins in stroke prevention: time to reconsider. The Lancet Neurology. 2017 Sep 1;16(9):750-60.
16. Niu X, Chen J, Wang J, Li J, Zeng D, Wang S, Hong X. A cross-sectional study on the relationship between homocysteine and lipid profiles among Chinese population from Hunan. Lipids. 2021 Jan;56(1):93-100.
17. Esse R, Barroso M, Tavares de Almeida I, Castro R. The contribution of homocysteine metabolism disruption to endothelial dysfunction: state-of-the-art. International journal of molecular sciences. 2019 Feb 17;20(4):867.
18. Perła-Kaján J, Jakubowski H. Dysregulation of epigenetic mechanisms of gene expression in the pathologies of hyperhomocysteinemia. International journal of molecular sciences. 2019 Jun 27;20(13):3140.
19. Kaplan P, Tatarkova Z, Sivonova MK, Racay P, Lehotsky J. Homocysteine and mitochondria in cardiovascular and cerebrovascular systems. International journal of molecular sciences. 2020 Oct 18;21(20):7698.
20. Antoniades C, Antonopoulos AS, Tousoulis D, Marinou K, Stefanadis C. Homocysteine and coronary atherosclerosis: from folate fortification to the recent clinical trials. Eur Heart J. 2008;30(1):6– 15.
21. Wierzbicki AS. Homocysteine and cardiovascular disease: a review of the evidence. Diab Vasc Dis Res. 2007;p. 143.
22. Wasilewska A, Narkiewicz M, et al. Is there any relationship between lipids and vitamin B levels in persons with elevated risk of atherosclerosis? Med Sci Monit 2003; 9:147-51.
23. Mahalle N, Kulkarni MV, Garg MK, Naik SS. Vitamin B12 deficiency and hyperhomocysteinemia as correlates of cardiovascular risk factors in Indian subjects with coronary artery disease. J Cardiol. 2013;61(4):289–94.
24. de Luis DA, Fernandez N, Arranz ML, Aller R, Izaola O, Romero E. Total homocysteine levels relation with chronic complications of diabetes, body composition, and other cardiovascular risk factors in a population of patients with diabetes mellitus type 2. J Diabetes Complications. 2005;19(1):42–6.
25. Watanabe M, Osada J, Aratani Y, Kluckman K, Reddick R, Malinow MR, Maeda N. Mice deficient in cystathionine beta-synthase: animal models for mild and severe homocyst (e) inemia. Proceedings of the National Academy of Sciences. 1995 Feb 28;92(5):1585-9.
26. Frauscher G, Karnaukhova E, Muehl A, Hoeger H, Lubec B. Oral administration of homocysteine leads to increased plasma triglycerides and homocysteic acid — additional mechanisms in homocysteine induced endothelial damage? Life Sci. 1995;57(8):813– 7.
27. Ali KM, Wonnerth A, Huber K, Wojta J. Cardiovascular disease risk reduction by raising HDL cholesterol - current therapies and future opportunities. Br J Pharmacol. 2012;167(6):1177–94.
28. Yadav AS, Bhagwat VR, Rathod IM. Relationship of plasma homocysteine with lipid profile parameters in ischemic heart disease. Indian J Clin Biochem. 2006;21(1):106–10.
29. Momin M, Jia J, Fan F, Li J, Dou J, Chen D, et al. Relationship between plasma homocysteine level and lipid profiles in a community- based Chinese population. Lipids Health Dis. 2017;16(1):54.
30. Ji C, Kaplowitz N. Hyperhomocysteinemia, endoplasmic reticulum stress, and alcoholic liver injury. World J Gastroenterol. 2004;10(12):1699–1708.