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Serum Homocysteine Level as a Predictive Marker in Patients of Coronary Artery Disease

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ABSTRACT
Coronary artery disease (CAD) is prevalent among Asian Indians, with acute myocardial infarction (AMI) rates rising in India and developing countries. India faces a growing cardiovascular disease burden due to multiple risk factors, including lifestyle (smoking, obesity, physical inactivity) and modifiable factors (lipid disorders, hypertension, insulin resistance). Non-modifiable factors include age, sex and genetics but these alone can't explain the high CAD rates among Indians. Our aim was to correlate Hyperhomocysteinemia with CAD risk factors. We included 189 in-patients in this cross-sectional study. We gathered clinical data and measured serum homocysteine levels. The study included patients with CAD, Ischemic Heart Disease, or a history of cardiac arrest. Males showed a higher CAD prevalence as compared to females. Hyperhomocysteinemia was found to be a significant risk factor in CAD patients. Our study highlights the independent association between elevated homocysteine levels and CAD risk. We established a positive correlation between hyperhomocysteinemia and major CAD risk factors, including Dyslipidemia, diabetes, hypertension and obesity, with statistical significance.

INTRODUCTION

Coronary artery disease (CAD) is highly prevalent among Asian Indians. India and other developing countries are witnessing a rapid increase in Acute Myocardial Infarction (AMI) and Ischemic Heart Disease. India stands at an epidemiological crossroads, poised for a substantial rise in cardiovascular diseases[1-3]. This susceptibility to Coronary Heart Disease arises from a convergence of various risk factors, including lifestyle-related ones like smoking, obesity and physical inactivity, as well as factors modifiable through lifestyle changes and pharmacotherapy, such as lipid disorders, hypertension and insulin resistance. Non-modifiable risk factors comprise age, sex and genetics, although these alone cannot account for the high rate of coronary heart disease. Among all ethnic groups, individuals of Indian origin have one of the highest CAD incidence rates[4-6].

Cardiovascular disease (CVD) is the foremost global cause of mortality, resulting in approximately 18 million deaths annually. Most of this burden is borne by lower- and middle-income countries, particularly in the Western Pacific Region of Asia. Epidemiological research has conclusively demonstrated that a small set of modifiable risk factors, including blood pressure, smoking, diabetes, total cholesterol and excess body weight, can explain up to 90% of all CVD cases. However, the relationship between these risk factors and coronary artery disease and stroke often varies by age and sex. Unfortunately, these differences are frequently overlooked in disease burden assessments, potentially leading to either overestimations or underestimations of disease burdens within specific population subgroups. This oversight can impact healthcare resource allocation.

MATERIAL AND METHODS

The study was conducted in a tertiary care hospital located in Central India. The research spanned two years and involved a total of 189 hospitalized patients. This research followed a cross-sectional design. We diligently collected detailed clinical histories and essential parameters from all relevant patients.

Inclusion criteria encompassed patients admitted to the hospital with a documented history of coronary artery disease or any previous cardiac arrest, as well as those with a prior record of medication or treatment for Angina/Myocardial Infarction or other cardiac conditions. Conversely, exclusion criteria applied to apparently healthy individuals without any known history of coronary heart disease or cardiac issues, individuals with renal diseases, thyroid complications, pregnant women, psoriasis, malignancy, epilepsy, or inflammatory bowel disease. Additionally, patients on specific oral medications such as methotrexate, carbamazepine, phenytoin, N_2O, or anticonvulsants were excluded from the study.

The assay procedure involved the collection of blood samples from all patients during their hospital admission using plain vacutainers or bulbs, followed by the prompt acquisition of fresh serum either through standing or centrifugation. Subsequently, a 20 mL serum sample was combined with 360 mL of Reagent 1 and the mixture was incubated at 37°C for 5 min. Following this incubation, 100 ml of Reagent 2 was added and the resultant mixture was subjected to analysis using the semiautomated biochemistry analyzer, with readings recorded after an additional 5 min.

RESULTS

Table 1 displays the age distribution of all study participants, with the majority falling within the 56-65 year age range. The study included 137 males (72.48%) and 52 females (27.52%) indicating a higher prevalence of CAD in males.

Table 2 presents the correlation between personal habits, specifically tobacco and alcohol consumption and serum homocysteine levels. The analysis revealed that neither of these habits exhibited a significant association with serum homocysteine levels.

Table 3 displays the correlation between co-morbidities and serum homocysteine levels. The results indicate that Diabetes mellitus, Dyslipidemia and Hypertension displayed a significant association with serum homocysteine levels.

Table 4 presents the correlation between BMI and serum homocysteine levels, revealing a significant association between BMI and serum homocysteine levels.

Table 1: Age distribution of study participants

Age group	No.	Percentage
25-35	11	5.82
36-45	25	13.23
46-55	44	23.28
56-65	53	28.04
66-75	43	22.75
75 and above	13	6.88
Total	189	100.00

Table 2: Correlation of alcohol and tobacco with homocysteine Levels

Tobacco/smoking	Increased homocysteine	Normal homocysteine	Total	p-value
Yes	9	35	44	0.32
No	43	102	145	
Total	52	137	189	
Alcohol				0.91
Yes	20	53	112	
No	32	84	77	
Total	52	137	189	

Table 3: Correlation of comorbidities and homocysteine levels

Diabetes mellitus	Increased homocysteine	Normal homocysteine	Total	p-value
Yes	39	73	112	<0.05
No	13	64	77	
Total	52	137	189	
Dyslipidemia				<0.05
Yes	35	38	73	
No	16	100	116	
Total	51	138	189	
Hypertension				<0.05
Yes	43	66	109	
No	9	71	80	
Total	52	137	189	

Table 4: Correlation of BMI and homocysteine Levels

BMI	Increased homocysteine	Normal homocysteine	Total	p-value
Normal	1	1	2	<0.05
Overweight	2	28	30	
Obese	49	108	157	
Total	52	137	189	

DISCUSSIONS

Over the past few decades, extensive efforts have been made to decrease the mortality rate associated with cardiovascular diseases. However, the effectiveness of prevention and treatment methods still falls short, especially among high-risk patient groups. Recent research has shifted its attention towards identifying new risk factors for CAD and improving prevention strategies[7-9]. Consequently, the current study aims to investigate the significance of serum homocysteine levels in relation to coronary artery disease. A total of 189 participants willingly took part in the study, all of whom either had a confirmed diagnosis of coronary artery disease or a documented history of cardiac conditions.

Numerous systematic reviews have conducted meta-analyses of prospective studies examining the association between serum cysteine levels and coronary artery disease[10-13]. In our study, majority of the cases were within the 56-65 years' age range. Males showed a higher prevalence of CAD compared to female gender. The study by Brilakis *et al*.[14], which involved 500 patients, reached the conclusion that a multivariate analysis taking into account factors such as age, gender, smoking, LDL, HDL, Lp (a), apo A1 and apo B did not show an independent association between quartiles of homocysteine and the odds ratio (OR) for coronary artery disease (CAD). It's important to note that these findings may not directly apply to our population due to potential differences in dietary habits and ethnic backgrounds when compared to Western studies. This study revealed a higher prevalence of CAD among males. This observation aligns with the findings from previous studies [15, 16], which also reported a similar male preponderance of CAD.

In Christine *et al*.[17], elevated serum homocysteine levels were observed in Type 2 diabetes mellitus patients compared to controls. The relationship between diabetes and coronary artery disease (CAD) varies across populations, with CAD incidence rates in diabetic patients ranging from 32-67%. Family history of CAD was present in 25.33% of the patients, categorized as a non-modifiable risk factor. Dyslipidemia, affecting approximately 350 million people worldwide, is a prevalent cardiovascular risk factor but its specific impact on CAD risk factors in angiographically confirmed CAD patients is not extensively studied. Smoking, identified as a risk factor in 38.67% of the patients, is responsible for about 20% of CAD-related deaths. Furthermore, smoking appears to have an inverse relationship with homocysteine bioavailability when folate intake is high[17-21]. Recent research highlights homocysteine as an independent predictor of vascular diseases, including coronary artery disease[22,23].

Our findings support the growing body of evidence indicating that elevated homocysteine levels are associated with a higher risk of coronary events. Specifically, hyperhomocysteinemia is identified as an independent risk factor for coronary events, both within the general population and among individuals with confirmed coronary artery disease based on angiography. This underscores the significance of elevated homocysteine levels as a potential contributor to coronary events in various patient groups.

CONCLUSION

This study identified a male predominance in coronary artery disease cases. It highlighted hyperhomocysteinemia as a significant risk factor, especially among younger individuals with CAD. Importantly, elevated homocysteine levels were found to be independently associated with CAD risk, regardless of other risk factors. The study also statistically confirmed a positive correlation between hyperhomocysteinemia and major traditional CAD risk factors, such as dyslipidemia, diabetes, hypertension and obesity.

REFERENCES

1. Enas, E.A. and J. Mehta, 1995. Malignant coronary artery disease in young Asian Indians: Thoughts on pathogenesis, prevention, and therapy. Clin. Cardiol., 18: 131-135.
2. Reddy, K.S., 1993. Cardiovascular diseases in India. World Health Stat. Q., 46: 101-107.
3. Bhat, K.S., 1988. Understanding Ischaemic heart disease. Health Adm., 9: 28-30.
4. Braunwald, E., A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo and J.L. Jameson, 2001. Harrison's Principles of Internal Medicine. 15th Edn., McGraw-Hill, ISBN-10: 0070072728, Pages: 2629.
5. Enas, E.A., S. Yusuf and J.L. Mehta, 1992. Prevalence of coronary artery disease in Asian Indians. Am. J. Cardiol., 70: 945-949.
6. Chadha, S.L., S. Radhakrishnan, K. Ramachandran, U. Kaul and N. Gopinath, 1990. Epidemiological study of coronary heart disease in urban population of Delhi. Indian J. Med. Res., 92: 424-430.
7. Naiksatam, M., V. Popat and A. Chavda, 2022. Serum homocysteine level as a predictive marker in patients of coronary artery disease: A study of 150 cases. Nat. J. Physiol., Pharm. Pharmacol., 12: 1352-1360.
8. Harst, P.V. and N. Verweij, 2018. Identification of 64 novel genetic loci provides an expanded view on the genetic architecture of coronary artery disease. Circulation Res., 122: 433-443.
9. Zhao, W., A. Rasheed, E. Tikkanen, J.J. Lee and A.S. Butterworth *et al*., 2017. Identification of new susceptibility loci for type 2 diabetes and shared etiological pathways with coronary heart disease. Nat. Genet., 49: 1450-1457.
10. Deng, J., X. Qian, J. Li, Y. Li, Y. Li and Y. Luo, 2018. Evaluation of serum cysteine-rich protein 61 levels in patients with coronary artery disease. Biomarkers Med., 12: 329-339.
11. Sinan, U.Y., I.P. Canbolat, O. Baydar, V. Oktay and G. Imre *et al*., 2013. Relationship between increased serum resistin level and severity of coronary artery disease. Angiology, 65: 239-242.
12. Creus, M., R. Deulofeu, J. Peñarrubia, F. Carmona and J. Balasch, 2013. Plasma homocysteine and vitamin b12 serum levels, red blood cell folate concentrations, C677T methylenetetrahydrofolate reductase gene mutation and risk of recurrent miscarriage: A case-control study in Spain. Clin. Chem. Lab. Med., 51: 396-399.
13. Xiao, Y., Y. Zhang, X. Lv, D. Su and D. Li *et al*., 2011. Relationship between lipid profiles and plasma total homocysteine, cysteine and the risk of coronary artery disease in coronary angiographic subjects. Lipids Health Dis., Vol. 10, No. 10. 10.1186/1476-511x-10-137.
14. Brilakis, E.S., J.P. McConnell, K.V. Ballman, G.G. Klee and P.B. Berger, 2002. Lack of association between plasma homocysteine and angiographic coronary artery disease in the era of fortification of cereal grain flour with folic acid. Atherosclerosis, 165: 375-381.
15. Mitchell, G.F., S.J. Hwang, R.S. Vasan, M.G. Larson and M.J. Pencina *et al*., 2010. Arterial stiffness and cardiovascular events: The framingham heart study. Circulation, 121: 505-511.
16. Tamura, A., T. Fujioka and M. Nasu, 2002. Relation of *Helicobacter pylori* infection to plasma vitamin B_{12}, folic acid, and homocysteine levels in patients who underwent diagnostic coronary arteriography. Am. J. Gastroenterol., 97: 861-866.
17. Christine, C.W., P. Auinger, A. Joslin and Y. Yelpaala, 2018. Vitamin B12 and homocysteine levels predict different outcomes in early Parkinson's disease. Mov. Disord., 33: 762-770.
18. Yaghootkar, H., R.A. Scott, C.C. White, W. Zhang and E. Speliotes *et al*., 2014. Genetic evidence for a normal-weight "metabolically obese" phenotype linking insulin resistance, hypertension, coronary artery disease, and type 2 diabetes. Diabetes, 63: 4369-4377.
19. Mahalle, N., M. Garg, S. Naik and M. Kulkarni, 2014. Study of pattern of dyslipidemia and its correlation with cardiovascular risk factors in patients with proven coronary artery disease. Indian J. Endocrinol. Metab., 18: 48-55.
20. Ginsberg, H.N., D.E. Bonds, L.C. Lovato, J.R. Crouse and M.B. Elam *et al*., 2007. Evolution of the lipid trial protocol of the action to control cardiovascular risk in diabetes (ACCORD) trial. Am. J. Cardiol., 99: S56-S67.
21. Goldenberg, I., M. Jonas, A. Tenenbaum, V. Boyko and S. Matetzky *et al*., 2003. Current smoking, smoking cessation, and the risk of sudden cardiac death in patients with coronary artery disease. Arch. Internal Med., 163: 2301-2305.
22. Lewis, S.J., S. Ebrahim and G.D. Smith, 2005. Meta-analysis of MTHFR 677C? T polymorphism and coronary heart disease: Does totality of evidence support causal role for homocysteine and preventive potential of folate? BMJ, Vol. 331, No. 7525. 10.1136/bmj.38611.658947.55.
23. Mizrahi, E.H., Y. Fleissig, M. Arad and A. Adunsky, 2005. Plasma homocysteine level and functional outcome of patients with ischemic stroke. Arch. Phys. Med. Rehabilitation, 86: 60-63.