International Journal of Clinical & Biomedical Research
Vol 7, Issue 4, 2021.

Sumathi Publications
Original Article

Homocysteine a non-conventional risk factor for vasculopathic patients

Dr Sunil Agarwal[1], Dr Deepak Kamat[2], Dr Pooja Shah[3], Dr Rahul Kunkulol[4]

[1]Assistant Professor, Department of Medicine, MIMER Medical College, Talegaon, Pune, Maharashtra
[2]Associate Professor, Obstetrics & Gynaecology, Rural Medical College, PIMS (D.U.), Maharashtra
[3]Resident, Orthodontics & Dentofacial Orthopaedics, Rural Dental College, PIMS (D.U.), Loni, Maharashtra
[4]Professor, Department of Pharmacology, Rural Medical College, PIMS (D.U.), Loni, Maharashtra

Abstract

Research is underway and many other factors are being identified, including homocysteine (Hcy). Since 1990, there has been an exponential increase in the number of publications on Hcy and coronary artery disease, suggesting elevated plasma Hcy as an independent risk factor. As a result, this study was conducted to determine the prevalence of a new risk factor (homocysteine) in the general population (both young and old), as well as any differences in prevalence rates (if any) between young (less than 45 years of age) and elderly (more than 45 years of age) patients with vasculopathy. This was a case control study done in the cardiology unit of Bharti Hospital, Pune. All the patients diagnosed as cases of vasculopathies, especially IHD/Stroke/DVT (n =75) were enrolled as cases for the study, and healthy volunteers of the same age and gender matched (n =75) were enrolled as controls and subjected to the following inclusion and exclusion criteria. All cases and controls were assessed for their homocysteine level on day 0 of admission by using the MEIA/FPIA Technique on IMX, Abbott, USA. The mean homocysteine level was 23.2499 (12.2739) in cases vs. 13.24 (3.0912) in controls, with a statistically significant 'p' value by unpaired 't' and Mann-Whitney statistics. Elevated Hcy levels above 15 mol/l were detected in 70% of cases and 22% of controls, respectively. On comparing homocysteine to individual vasculopathy, it was found that homocysteine was a more significant risk factor in IHD > stroke >DVT.

KEYWORDS: Homocysteine; Vasculopathy; Ischaemic heart disease; Stroke; Deep vein thrombosis; Risk Factor

Introduction

Atherosclerotic disease of the coronary, peripheral, and cerebrovascular systems continues to be a serious health burden in both industrialized and developing countries' adult populations. Controlling traditional risk factors has resulted in a decrease in the incidence of coronary artery disease in developed countries [1]. However, despite increasing risk factor management in the general population, not all patients have been able to avoid or stop the course of coronary artery disease or cerebrovascular stroke.

Although the frequency of vasculopathy increases with age, vasculopathy in the young is essential because the aetiology and management differ, and it plays a vital part in any country's progress, especially in a growing country like ours [2]. The etiology of coronary artery disease in adolescents and young adults is unknown. Coronary artery disease in the young is described as coronary artery disease in people under the age of 45 [3]. In Asian Indians, 12- 16 percent of all instances of coronary artery disease occur in people under the age of 45, compared to only 2-5 percent of people in the West in the same age group [4]. Because of severe atherosclerosis and multivessel disease, young Asian Indians with coronary artery disease typically have a worse prognosis, a pattern

Correspondence: Dr. Deepak Kamat, Department of Obstetric Gynaecology, Rural Medical College Pravara Institute of Medical Sciences (Deemed to be University), Loni, Maharashtra. Email id: researchcell@pmtpims.org

eISSN: 2395-0471
pISSN: 2521-0394

© Authors; 2021. (CC BY-NC-SA 4.0)
This is an Open Access article which permits unrestricted non-commercial use, provided the original work is properly cited.

previously found mainly in the elderly [5].

Thus, there was a need to look beyond conventional risk factors. Recently, research is underway and many other factors are being identified, including homocysteine (Hcy). McCully, a young Harvard Pathologist at the time, was the first to make the clinical connection between elevated plasma homocysteine levels and vascular disease [6]. Homocysteine is a sulfhydryl - containing amino acid derived from the metabolic demethylation of dietary methionine. Homocysteine has a key place in between Folate cycle and the activated methyl cycle [7]. Homocysteine is also a potent mitogen, leading to marked rise in vascular smooth muscle proliferation [8].

Homocysteine also affects the coagulation system. A high level of homocysteine reduces protein C activation, thus inhibiting its anticoagulant activity [9].

As a result, this study was conducted to determine the prevalence of a new risk factor (homocysteine) in the general population (both young and old), as well as any differences in prevalence rates (if any) between young (less than 45 years of age) and elderly (more than 45 years of age) patients with vasculopathy.

AIMS AND OBJECTIVES:

To find out the mean Homocysteine levels in patients suffering from vasculopathy- IHD/ stroke/DVT and compare with healthy controls with respect to young age (<45 years) and the elderly (>45 years).

Material And Methodology

Study design: Case control observational study

Ethical approval: Study was approved by the Institutional Ethics Committee

Study location: Study was conducted at Cardiology unit of Bharti Hospital, Pune

Study duration: 03 years

Inclusion criteria: Adult patients above 20 years of either gender diagnosed as cases of vasculopathies, especially IHD/ Stroke/ DVT (n=75) were enrolled as cases for the study, and healthy volunteers of the same age and gender matched (n =75) were enrolled as controls and subjected to the following inclusion and exclusion criteria.

Exclusion criteria: Patients suffering from cerebrovascular disease due to trauma, tumours, atrial fibrillation, haemorrhagic diathesis, pernicious anaemia, hypothyroidism, and patients who are known cases of vasculopathies on antiplatelets, fibrinolytics, corticosteroids, and anticoagulants were excluded from the study

Sample size: Obe hundred fifty

Methodology: All the eligible cases and controls were assessed for homocysteine levels along with the routine protocol of history, general examination, and systemic examination, and cases were additionally investigated as per the decided protocol for the type of vasculopathy. All cases and controls were assessed for their homocysteine levels on day 0 of admission by using the MEIA/FPIA Technique on IMX, Abbott, USA. The mean of homocysteine was compared in both the cases and the controls and was subjected to unpaired 't' and Mann-Whitney test statistics.

Results

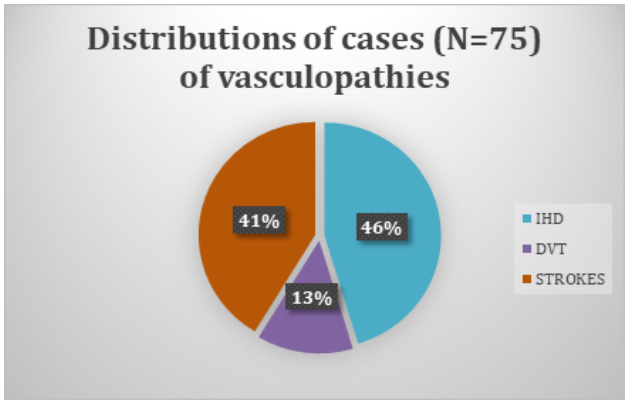

Fig 1. Distributions of cases(N=75) of vasculopathies

Total 75 patients of vasculopathies of which 31 had stroke, 10 had DVT, and 34 had IHD whereas 75 healthy individuals were the controls.

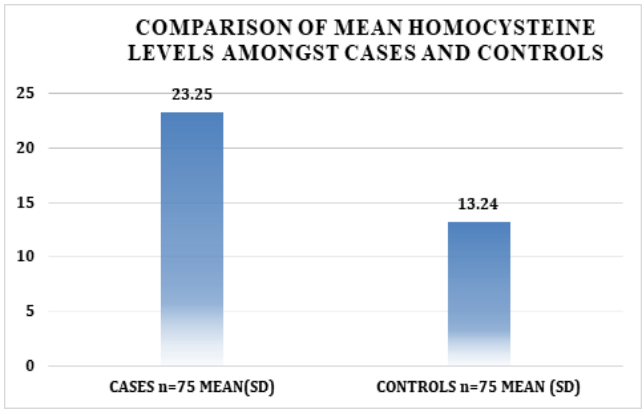

Fig 2. Comparison of mean Homocysteine levels amongst Cases and controls

In the present study, the mean homocysteine level of 23.2499 (12.2739) in cases vs 13.24 (3.0912) in controls with a statistically significant 'p' value by unpaired 't' and Mann- Whitney statistics.

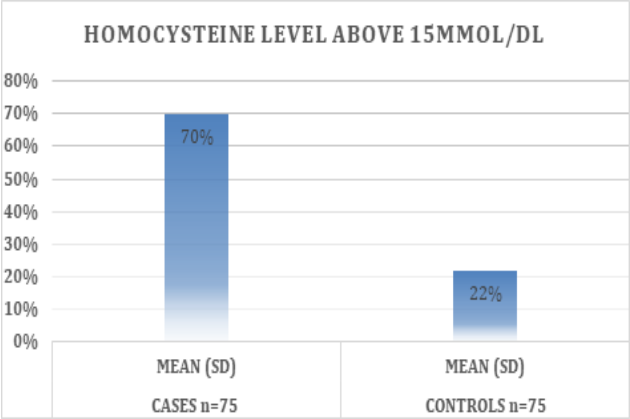

Fig 3. Homocysteine levels

70% Cases had Homocysteine level above 15µmol/dl in comparison only 22% controls had levels above 15µmol/dl with a statistically significant 'p' value by unpaired 't' and Mann-Whitney statistics.

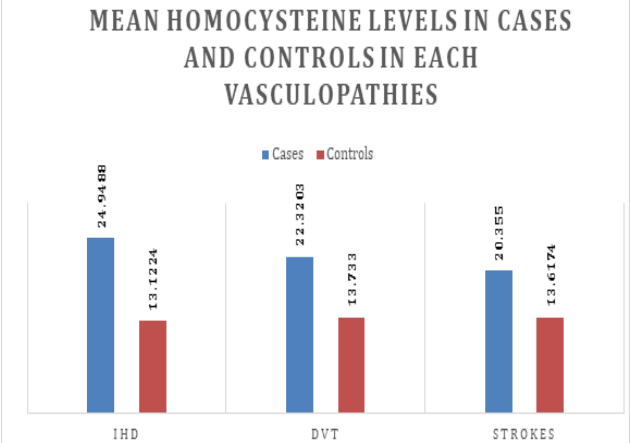

Fig 4. Mean Homocysteine levels in Cases and controls in each vasculopathies

On comparing Homocysteine individual vasculopathy, it was found that homocysteine was a more significant risk factor in IHD >Stroke> DVT.

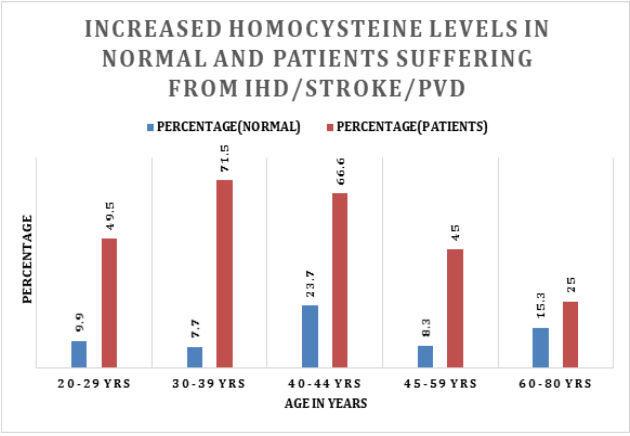

Fig 5. Homocysteine was compared in the different age groups in both the cases and the control group.

Homocysteine was compared in the different age groups in both the cases and the control group and the study revealed that homocysteine level was found elevated in all the age group but more in age 30 to 44 years as compared to other age groups.

Discussion

A total of 150 cases (75 patients + 75 controls) were included in this study. Of these 75 patients, 31 had strokes, 10 had DVT, and 34 had IHD. In the 3-year span between 2016 to 2019 most cases were of stroke and IHD, signifying a high level of arterial thrombus as compared to DVT, where there were only 10 patients, signifying a low level of venous thrombosis cases.

In the present study, elevated Hcy levels above 15 µmol/1 were detected in 70% of cases and 22% of controls, with a statically significant 'P' value < 0.01 by unpaired 't' And Mann-Whitney test statistics with a mean SD of 23.25 (12.273) in cases versus 13.24 (3.0912) in controls.

Elevated Hcy levels were found by Robert Clark et al. [9,10 with a mean of 18.70 in cases/13.40 in the control of the IHD group; a mean of 20.40/13.40 in the stroke group; and 15.80/13.40 in the DVT group. In the present study, the mean of elevated Hcy levels in the IHD group as compared to the control group was 24.94 [14]. In the stroke group it was 22.32/13.61, whereas in the DVT it was 20.53/13.73. Smitha Ghee et al. [11] did not find a significant difference in increased Hcy levels in IHD patients as compared to controls.

On comparing Hcy in individual vasculopathy, it was found that Hcy was a more significant risk factor in IHD > stroke > DVT with a mean value of 24.95 > 22.35 > 20.36, respectively, and it was found that there was no significant difference in the young and elderly. It was equally prevalent in both the age groups.

The results of our study does not correlate with other studies where increased Hcy was found in the young, [12,13 as these studies did not involve elderly patients for comparison. Results of our study in patients with DVT are comparable with studies done by Robert Clarke10, which showed mean Hcy levels in cases and control of 15.80/13.40, R. J Valentine et al.[14], 15.90/14.70, and our results showed levels of 20.35/13.73. All the above studies showed similar increases in homocysteine levels, although the values varied due to variation in sample size. Our findings in patients with IHD are comparable to those of Robert Clarke [10,15], who found a mean Hcy level in cases and controls of 18.70/13.40, Smitha Gheye et al. [16], 21.50/19.70, and our findings of 24.94/13.12.Whereas in stroke patients, the

results of Robert Clarke 10 (20.40/13.40) and our study (22.32/13.61) are almost similar.

The odds ratio of Hcy in all the three vascular diseases in the present study was compared with the controls, and the results were compared with the Boushey et al. meta-analysis of 27 studies [17]. From this comparison, it was concluded that there was an increased risk of vascular disease with homocysteinamia.

Conclusion

The prevalence of homocysteine levels in patients suffering from vasculopathy (IHD, stroke, or DVT) was found to be significantly higher as compared with healthy controls. Hcy was significant in both the younger (45-year-old) and elderly (> 45-year-old) groups. was a more important risk factor in IHD > stroke >DVT. In view of the above significant results, it is suggested that due consideration may be given to the estimation of these new risk factors, homocysteine, along with conventional ones, in every case of vasculopathy.

Conflict of interest : Nil
Source of funding : Nil

References

1. McKeigue PM, Miller GJ, Marmot MG. Coronary heart disease in South Asians overseas: a review. J Clin Epidemiol. 1989;42(7):597-609.
2. Nelson RH. 'Hyperlipidemia as a risk factor for cardiovascular disease' Prim Care. 2013;40(1):195-211.
3. Lowry PJ, Glover DR, Mace PJ, Littler WA. Coronary artery disease in Asians in Birmingham [internet]. Br Heart J. 1984;52(6):610-3.
4. Hughes LO, Raval U, Raftery EB. First myocardial infarctions in Asian and white men [internet]. BMJ. 1989;298(6684):1345-50.
5. Hughes LO. Insulin, Indian origin and ischaemic heart disease. Int J Cardiol. 1990;26(1):1-4.
6. McCully KS. 'Vascular pathology of homocysteinemia: implications for the pathogenesis of arteriosclerosis'. Am J Pathol. 1969;56(1):111-28.
7. Finkelstein JD. Methionine metabolism in mammals. J Nutr Biochem. 1990;1(5):228-37.
8. Tsai JC, Perrella MA, Yoshizumi M, Hsieh CM, Haber E, Schlegel R, Lee ME. Promotion of vascular smooth muscle cell growth by homocysteine: a link to atherosclerosis. Proc Natl Acad Sci U S A. 1994;91(14):6369-73.
9. 9. Lentz SR, Sadler JE. Inhibition of thrombomodulin surface expression and protein C activation by the thrombogenic agent homocysteine. J Clin Invest. 1991;88(6):1906-14.
10. Clarke R, Daly L, Robinson K, Naughten E, Cahalane S, Fowler B, Graham I. Hyperhomocysteinemia: an independent risk factor for vascular disease. N Engl J Med. 1991;324(17):1149-55.
11. Jain S, Ram H, Kumari S, Khullar M. Plasma homocysteine levels in Indian patients with essential hypertension and their siblings. Ren Fail. 2003;25(2):195-201.
12. McCully KS, Wilson RB. Homocysteine theory of arteriosclerosis. Atherosclerosis. 1975;22(2):215-27.
13. Van den Berg M, Boers GH, Franken DG, Blom HJ, Van Kamp GJ, Jakobs C, Rauwerda JA, Kluft C, Stehouwert CD. Hyperhomocysteinaemia and endothelial dysfunction in young patients with peripheral arterial occlusive disease. Eur J Clin Investig. 1995;25(3):176-81.
14. Valentine RJ, Kaplan HS, Green R, Jacobsen DW, Myers SI, Clagett GP. Lipoprotein (a), homocysteine, and hypercoagulable states in young men with premature peripheral atherosclerosis: A prospective, controlled analysis. J Vasc Surg. 1996;23(1):53-61
15. Clarke. booksellers, Cincinnati. Robert Clarke & Co. CO: RC & Robert Clarke & Co.; 1888's Catalogue of Works on Political Economy. Finance. Political and social science, etc: classified by subjects; 1888. 78 p.
16. Gheye S. homocysteine levels in Indians. hypertension India. 2001;15/3:18-21
17. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA. 1998;279(18):1477-82.