Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

Original Research Article

A Clinical Study of the Prevalence of Hyperhomocysteinemia in Cases of DVT

Dr. Vasanth Kumar Suram[1], Dr. Gadiga Srikanth Goud[2], Dr. Ravindar Kumar Gadi[3], Dr. Jilla Naganna[4], Dr. Jangam Sukesh Kumar[5]

[1]Assistant Professor, Dept of General Medicine, Gandhi Medical College and Hospital, Secunderabad, Telangana State.

[2]Assistant Professor, Dept of General Medicine, Gandhi Medical College and Hospital, Secunderabad, Telangana State.

[3]Assistant Professor, Dept of General Medicine, Gandhi Medical College and Hospital, Secunderabad, Telangana State.

[4]Assistant Professor, Dept of General Medicine, Gandhi Medical College and Hospital, Secunderabad, Telangana State.

[5] Consultant Physician, Vignesh Hospital, Nakkal Road, Vijayawada, Andhra Pradesh.

Corresponding Author: Dr. Jilla NagannaE-mail: nagan99@gmail.com

Abstract

Background: Hyperhomocysteinemia is a known risk factor for the development of deep vein thrombosis. There are several studies have been conducted in western countries to know the prevalence of hyperhomocysteinemia in patients with DVT and the general population. There is no documented literature on the prevalence of hyperhomocysteinemia in the Indian population. Thus, this study aimed to determine the prevalence of hyperhomocysteinemia in cases of DVT in our population.

Methods**:** All patients with deep vein thrombosis confirmed by Doppler ultrasound were included in the study. Demographic profile and details of the patient like name, age, sex, inpatient number, history of smoking, DM, HTN, and IHD were recorded on a pre-structured proforma. 2 ml of fasting venous blood sample was collected in EDTA bulb from the cubital vein and sent for serum homocysteine estimation to the biochemistry laboratory. The ELISA method was used for the estimation of serum homocysteine levels.

Results: Out of n=60 cases higher levels of homocysteine were detected in n=26(43.33%) cases. Out of n=25 males, n=10(40%) were high homocysteine levels and out of n=35 females, n=16(45.71%) were with high levels of homocysteine. Based on the severity of hyperhomocysteine levels cases were divided into moderately high levels with values > 15 µmol/L. Intermediate with values > 30 µmol/L and severe with values >100 µmol/L of homocysteine. 10% of the cases were in the moderate category, 20% cases in the intermediate category and 13.33% of cases in this study were in a severe category.

Conclusion: prevalence of hyperhomocysteinemia was 43.33% in cases of DVT. Smoking was significantly associated with elevated hyperhomocysteinemia. Low-dose folic acid, pyridoxine, and cobalamin are low-cost, low-risk pharmacological alternatives for lowering and maintaining homocysteine levels in at-risk populations.

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

Keywords: Prevalence,Hyperhomocysteinemia, Deep vein thrombosis, Risk factors

Introduction

Deep vein thrombosis (DVT) is a common yet difficult-to-diagnose condition that can cause pain and death if not properly diagnosed and treated. When venous thrombi break off and create pulmonary emboli, which travel to and block the arteries of the lung, death might result. DVT and pulmonary embolism (PE) are most commonly associated with ill, hospitalized individuals, although they can also afflict otherwise healthy people who are ambulatory. Because venous thrombosis is difficult to diagnose clinically, these hospitalized instances are likely only the beginning. Unfortunately, PE and DVT have a high fatality rate, and those who are afflicted have a worse chance of surviving than those who are not. For some years, a link has been established between the risk of venous thromboembolism and a hypercoagulable condition. Recent advancements in thrombosis research and laboratory medicine have resulted in an ever-growing list of particular test abnormalities that may predispose persons to venous thromboembolism. Mild hyperhomocysteinemia has been linked to the development of atherosclerosis and vascular disease. [1, 2] Half of the vascular consequences in classic homocystinuria are venous but it was unclear if moderate hyperhomocysteinemia is also a risk factor for venous thrombosis until recently. [3-5] Falcon et al., discovered that hyperhomocysteinemia was a risk factor for thrombosis in persons under the age of 40 in a case-control study. [6] Hyperhomocysteinemia has recently been discovered to be a risk factor for recurrent venous thrombosis in individuals aged 20 to 70, as compared to controls from the general population. [7] Several mechanisms may lead to the development of hyperhomocysteinemia which includes deficiencies in folate, Vitamin B6, and vitamin B12. [8, 9] A reduced activity of methylenetetrahydrofolate reductase or other enzyme defects within the hyperhomocysteinemia pathway. [10, 11] Whether hyperhomocysteinemia behaves as a biological marker or a direct etiologic agent in the development of thrombosis remains to be established. The findings confirm the idea that moderate hyperhomocysteinemia is a risk factor for venous thrombosis, although the trials were not designed to evaluate the risk in the general population. Although research exists that shows the prevalence of hyperhomocysteinemia in patients with DVT in the western population, there are no studies in the literature that show the frequency of hyperhomocysteinemia in patients with DVT in the Indian community. Thus, the present study was undertaken to detect the prevalence of hyperhomocysteinemia in patients with DVT coming to our hospital.

Material and Methods

This study was conducted in Gandhi Medical College, Secunderabad over a period of 18 months from Jan 2018 to June 2019 after obtaining approval from the institutional ethics committee, written informed consent was taken from all the patients who were included in the study.

Inclusion criteria:

1. All patients with deep vein thrombosis confirmed by Doppler ultrasound were
2. included in the study.
3. Males and Females
4. Aged 18 and above
5. Voluntarily willing to participate in the study

Exclusion criteria:

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

1. Patients with a previous history of prolonged immobilization i.e., post-partum,
2. post-major surgical procedures, trauma, obesity.
3. Patients using oral contraceptive pills and hormonal replacement therapy.

During the course of the study, all patients with Doppler ultrasound proved deep vein thrombosis was included in the study. Demographic profile and details of the patient like name, age, sex, inpatient number, history of smoking, DM, HTN, and IHD were recorded on a pre-structured proforma. 2 ml of fasting venous blood sample was collected in EDTA bulb from the cubital vein and sent for serum homocysteine estimation to the biochemistry laboratory. The ELISA method was used for the estimation of serum homocysteine levels. Hyperhomocysteinemiawas defined as a serum homocysteine level of more than 16.0 in the patients.

Statistical analysis: All the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 22 (Chicago, IL, USA). The descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Differences between the two groups were done using the Chi-Square test with Yate's correction a p-value of < 0.05 was taken as significant.

Results

Out of the total n=60 cases included in study n=35(58.33%) were females and n=25(41.67%) were males. The youngest among the male was 21 years old and the oldest male was 68 years old. The mean age of male patients was 38.5 ± 7.5 years. Similarly in females, the youngest case was 35 years old and the oldest case was 69 years old. The mean age of females was 42.2 ± 8.5 years. The overall mean age of the cohort was 41.35 ± 8.5 years. The detailed age-wise distribution of cases in the study is given in table 1.

Table 1: Age-wise distribution of the cases included in the study

Age group (years)	*Frequency*	*Percentage*
18 - 20	2	03.33%
21 - 30	10	16.67%
31 - 40	19	31.66%
41 - 50	15	25.00%
51 – 60	8	13.33%
61 - 70	6	10.00%
Total	60	100.0%

The estimation of risk factors for the DVT was done in the study out of a total of n=60 cases n=38(63.33%) showed the presence of one of the risk factors for DVT. The distribution of risk factors in the cases is depicted in table 2. All the cases of smoking n=12 were found in males and none in females. In the hypertension category, the existence of hypertension was found in n=6 females and n=5 males. The prevalence of diabetes was found in n=8 cases out of which n=5 were males and n=3 were females. The risk factor of IHD was found in n=7 cases out of which n=6 cases were males and n=1 cases were females. The P-value for the distribution of risk factors in the males was significant in patients with IHD wherein the P-value was <0.005.

Table 2: Risk factor evaluation in the cases of study

Risk Factors		*Frequency*	*Percentage*
Smoking	Present	12	20.00

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

	Absent	48	80.00
Hypertension	Present	11	18.33
	Absent	49	81.67
Diabetes Mellitus	Present	08	13.33
	Absent	52	86.67
Ischemic Heart Disease	Present	07	11.67
	Absent	53	88.33

The doppler study of DVT showed the most involved vein was the Right Deep Femoral vein in 33.33% of cases followed by the right common femoral vein in 30.00% of cases and left deep femoral vein in 23.33% of cases and left common femoral vein in 13.33% cases given in table 3.

Table 3: Doppler study of DVT and its distribution in the cases

		Frequency	*Percentage*
Doppler study	DVT Left Common Femoral Vein	08	13.33
	DVT Left Deep Femoral Vein	14	23.33
	DVT Right Common Femoral Vein	18	30.00
	DVT Right Deep Femoral Vein	20	33.33
Total		60	100.00

Out of n=60 cases, higher levels of homocysteine were detected in n=26(43.33%) cases. Out of n=25 males, n=10(40%) were high homocysteine levels and out of n=35 females, n=16(45.71%) were with high levels of homocysteine. Based on the severity of hyperhomocysteine levels cases were divided into moderately high levels with values > 15 µmol/L. Intermediate with values > 30 µmol/L and severe with values >100 µmol/L of homocysteine. 10% of the cases were in the moderate category, 20% cases in the intermediate category and 13.33% of cases in this study were in the severe category the details have been depicted in table 4. The sex-wise distribution of the hyperhomocysteinemia in comparison with males and females revealed p-values <0.05 hence considered significant.

Table 4: Serum homocysteine levels and their distribution gender wise

	Category	*Gender*			
		Females	*Males*	*Total*	*Percentage*
Serum Homocysteine levels	Normal (< 15 µmol/L)	19	15	34	56.67
	Moderate (15 -30 µmol/L)	3	3	06	10.00
	Intermediate (30 - 100 µmol/L)	8	4	12	20.00
	Severe (>100 µmol/L)	5	3	08	13.33
Total		35	25	60	100.00

Discussion

Homocysteine is an amino acid that is produced when methionine is demethylated inside the cell. Hyperhomocysteinemia is defined by a rise in homocysteine levels in the blood. Myocardial infarction, peripheral artery thrombosis, deep vein thrombosis, and pulmonary embolism are all regarded to be modifiable risk factors. [5, 6, 12] The majority of publications on artery disease mention a link to a modestly elevated homocysteine level. In contrast, there are few contradictory studies on venous system thrombosis linked to homocysteine levels. [13-

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

[17] Hyperhomocysteinemia can be caused by genetic abnormalities in homocysteine metabolism enzymes such as cystathionine ß-synthase (CBS), and methionine synthase (MS), and N5, N10-Methylenetetrahydrofolate Reductase (MTHFR) or cofactor deficiencies (Vitamin B6, Vitamin B12, or co-substrate Vitamin B9). [14] Hyperhomocysteinemia has been linked to a higher risk of deep vein thrombosis. Hyperhomocysteinemia is common in DVT patients, according to the literature. Homocysteine levels were found to be elevated in 40% of individuals with vascular disease and 35% of patients with venous thromboembolism 18. Simioni et al., [7] found that hyperhomocysteinemia was prevalent in 25% of the participants in their case-control study. The frequency of hyperhomocysteinemia was found to be 10% in another research by Den Heijer M et al., [6] The prevalence of hyperhomocysteinemia in spontaneous DVT cases was found to be % in our study, whereas the prevalence of hyperhomocysteinemia in n=26(43.33%) of cases. We in the current study measured the fasting homocysteine levels. It has been said that fasting homocysteine levels is a satisfactory method for testing homocysteine defects because of its ease of performance and better accuracy as compared to the measuring homocysteine levels postprandially. [5] Hyperhomocysteinemia was revealed to be a risk factor for thrombosis in persons under the age of 40 by Falcon et al., [4] When compared to controls from the general population, hyperhomocysteinemia is a risk factor for recurrent venous thrombosis in individuals aged 20 to 70. The frequency of hyperhomocysteinemia among the different age groups had no statistical significance in our investigation. IHD was significant in the distribution of risk variables in the two groups, with a P-value of 0.016. Hyperhomocysteinemia has also been linked to thrombosis of the arteries. [5, 6, 18] It has been proven to be a risk factor for atherosclerosis and vascular disease. The link between moderate hyperhomocysteinemia and venous thrombosis is comparable to the link between hyperhomocysteinemia and arterial vascular disease documented. [7, 19] As a result, there is a statistically significant link between hyperhomocysteinemia and IHD in our study. Smoking is an established risk factor for hyperhomocysteinemia, this investigation found to be a statistically significant link between the two.

Conclusion

Within the limitations of the current study, it can be concluded that the prevalence of hyperhomocysteinemia was 43.33% in cases of DVT. Smoking was significantly associated with elevated hyperhomocysteinemia. Low-dose folic acid, pyridoxine, and cobalamin are low-cost, low-risk pharmacological alternatives for lowering and maintaining homocysteine levels in at-risk populations. In all cases of deep vein thrombosis, homocysteine levels should be measured, and patients with hyperhomocysteinemia should begin long-term or lifelong folic acid and vitamin B12 treatment.

References

1. Undas A, Brozek J, Szczeklik A. Homocysteine and thrombosis: from basic science to clinical evidence. Thromb Haemost 2005; 94:907–15.
2. Rees MM, Rodgers GM. Homocysteinemia: association of a metabolic disorder with vascular disease and thrombosis. Thromb Res 1993; 71:337–59.
3. Mudd SH, Skovby F, Levy HL. The natural history of homocystinuria due to cystathionine beta-synthase deficiency. Am J Hum Genet 1985; 37:1–31
4. Falcon CR, Cattaneo M, Panzeri D, et al. High prevalence of hyperhomocysteinemia in patients with juvenile venous thrombosis. Arterioscler Thromb 1994; 14:1080–83.
5. Den Heijer M, Blom HJ, Gerrits WBJ. Is hyperhomocysteinemia a risk factor for recurrent venous thrombosis? Lancet 1995; 345:882–85.
6. Den Heijer M, Koster T, Blom HJ. Hyperhomocysteinemia as a risk factor for deep-vein

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 04, 2022

thrombosis. N Engl J Med 1996; 334:759–62.
7. Simioni P, Pradoni P, Burlina A, et al. Hyperhomocysteinemia and deep-vein thrombosis. A case-control study. Thromb Haemost 1996; 76(6):883–86.
8. Ubbink JB, Vermaak WJ, Van der Merwe A, Becker PJ. Vitamin B-12, Vitamin B-6 and folate nutritional status in men with hyperhomocysteinemia. Am J Clin Nutr 1993; 57:47-5.
9. Robinson K, Mayer EL, Miller DP, et al., Hyperhomocysteinemia and low pyridoxal phosphate: common and independent reversible risk factors for coronary artery disease. Circulation 1995; 92: 2825-30.
10. Kang SS, Passen EL, Ruggie N, Wong PW, Sora H. Thermolabile defect of methylenetetrahydrofolate reductase in coronary artery disease. Circulation 1993; 88: 1463-69.
11. Berg k, Malinow MR, Kierulf P, Upson B. population variation and genetics of plasma homocysteine level. Clin Genet 1992; 41:315-21.
12. Ravari H, Zafarghandi MR, Alvandfar D, Saadat S. Serum homocysteine in deep venous thrombosis, peripheral atherosclerosis and healthy Iranians: A case-control study. Pak J Biol Sci. 2009;12(14):1019–24.
13. Clarke R. Lowering blood homocysteine with folic acid based supplements: a meta-analysis of randomized trials. BMJ. 1998; 316:894–88.
14. Kang SS, Wong PWK. Genetic and nongenetic factors for moderate hyperhomocysteinemia. Atherosclerosis. 1994; 119:135–88.
15. Ekim M, Ekim H, Keser Yilmaz Y, et al. Study on relationships among deep vein thrombosis, homocysteine, and related B group vitamins. Pak J Med Sci. 2015; 31(2):398–02.
16. Ducros V, Barro C, Yver J, Pernod G, Polack B, et al. Should Plasma Homocysteine Be Used as a Biomarker of Venous thromboembolism? A Case-Control Study. Clin Appl Thromb Hemost. 2009;15(5):517–22.
17. Herrmann M, Whiting MJ, Veillard A, Ehnholm C, Sullivan DR, Keech AC. Plasma homocysteine and the risk of venous thromboembolism: insights from the field study. Clin Chem Lab Med. 2012; 50: 2213–19.
18. Rosen P, Barkin RM. Emergency Medicine: Principles and Practice. Chapter 107, Vol 3. 4th ed. St. Louis, Mosby 1998; P. 1123–54.
19. Selhub J, Jacques PF, Bostom AG. Association between plasma homocysteine concentrations and extracranial carotid artery stenosis. N Engl J Med 1995; 332:286–91.