

Original research article**A study of homocysteine in patients with deep vein thrombosis****¹Dr. Abid Abdul Rahiman, ²Dr. Sanjay Nagappa Koppad, ³Dr. Christopher Sam Thomas**¹Junior Resident, Department of General Surgery, Yenepoya Medical College and Hospital, Mangalore, Karnataka, India²Professor, Department of General Surgery, Yenepoya Medical College and Hospital, Mangalore, Karnataka, India³Assistant Professor, Department of General Surgery, Yenepoya Medical College and Hospital, Mangalore, Karnataka, India**Corresponding Author:**

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Abstract

Several theoretical procedures have been proposed to elucidate the mechanisms by which elevated levels of homocysteine contribute to the development of venous thrombosis and atherosclerosis. One of the several possibilities posits that homocysteine exerts a deleterious effect on the arterial endothelium, hence initiating the process of clot formation. Another mechanism postulated is that when methionine metabolism is faulty, there is aberrant methylation of the DNA and cell membranes. The condition of hyperhomocysteinemia has been seen to interfere with the normal functioning of the methionine metabolic pathway. Furthermore, it has been emphasised that individuals with atypical levels of vitamin B12, B6, and folic acid have elevated concentrations of homocysteine, resulting in vascular endothelial alterations. The thrombotic risk associated with hyperhomocysteinemia of various aetiologies remains uncertain. The objective of this study is to investigate the correlation between blood homocysteine levels and the risk of venous thrombosis.

Keywords: Homocysteine, deep vein thrombosis, costal, Karnataka**Introduction**

Deep venous thrombosis (DVT) is a medical condition characterised by the existence of a clearly defined echogenic thrombus inside the deep venous system of the human body. Deep vein thrombosis (DVT) has the potential to manifest in any of the veins within the deep venous system. However, the deep veins of the lower leg are the most often afflicted locations in cases of DVT. Therefore, in a broad sense, when discussing deep vein thrombosis (DVT), it commonly pertains to the involvement of the deep veins located in the leg ^[1]. Common manifestations of deep vein thrombosis (DVT) encompass localised discomfort and edoema, predominantly observed in the calf region. In around 50% of instances, deep vein thrombosis (DVT) may not exhibit consequences. However, in the remaining cases, there are potentially lethal complications such as pulmonary embolism. This occurs when the thrombus becomes dislodged from the veins in the lower limbs and migrates to the major pulmonary arteries. There are several predisposing variables that contribute to the development of venous thrombosis. However, the fundamental processes behind its creation entail a combination of restricted blood flow, an increased tendency to form clots, and damage to the endothelium lining the veins. According to estimates, the incidence of deep vein thrombosis (DVT) in the United States is around one case per one thousand persons each year. Additionally, there is a notable prevalence of consequences, such as pulmonary embolism, occurring in around two-thirds of those who have experienced deep vein thrombosis ^[1]. Long-term implications of deep vein thrombosis (DVT) include the development of chronic venous insufficiency and venous ulcers, along with related morbidity and expense ^[1].

Deep vein thrombosis (DVT) is a medical condition characterised by a notable tendency for recurrence, particularly among those who possess certain predisposing variables that cannot be modified. The prevalence of such factors ranges from 12% to 30% ^[2]. To mitigate the likelihood of a reoccurrence, medical practitioners frequently administer anticoagulation medication for a duration of 3-6 months subsequent to an episode of venous thrombosis ^[3-5]. In this study, we aim to investigate the effects of a particular intervention on cognitive development in the elevation of Homocysteine levels in the serum has been well reported as a significant risk factor for the development of deep vein thrombosis (DVT). Homocysteine is an amino acid that contains sulphur and serves as an intermediate product in the metabolic pathway of methionine. The variables influencing homocysteine levels encompass genetic and physiological factors, lifestyle choices, nutritional intake, diverse medical conditions, and drug usage.

Classical hereditary homocystinuria, a recognised medical condition characterised by elevated homocysteine levels over 100µmol/l, has been shown as a significant risk factor for both arterial and venous thrombosis. The user did not provide any text to rewrite.

The renal functions and synthesis of creatinine have an impact on the levels of homocysteine. Individuals who adhere to a highly nutritious lifestyle and maintain adequate intake of vitamins and essential elements may exhibit reduced levels of homocysteine.

Aim of the study

To measure the levels of homocysteine in patients with deep vein thrombosis.

Materials and Methods

Study design: Cross Sectional study.

Study setting

Yenepoya Medical College Hospital (YMCH) is a 900 bedded tertiary care teaching hospital situated in Deralakatte, a suburban locality of Mangaluru, Dakshina Karnataka. It provides general and specialist healthcare to the coastal and central parts of Karnataka and northern part of Kerala.

Study population

- Patients diagnosed with Deep Vein Thrombosis.

Study period: The study was done between the time period of January 2020 and October 2021.

Inclusion criteria

- Cases diagnosed with deep vein thrombosis.
- Cases who had given written informed consent for the study.

Exclusion criteria

- Patients who had discontinued anti coagulation therapy.
- Patents already on vitamin B supplementation.

Sampling procedure: Simple Random Sampling.

Randomization: Nil.

Method of collection of data

- With the above specified information and considering 5% level of significance and 43% of prevalence; according to the article Kopturk *et al.*^[10], with 13% of margin of error sample size is 56.
- $n = Z^2 \frac{1 - \alpha}{\alpha} pq \div d^2$
- $n = 56$
- **Type of study:** Prospective study.
- **Samples to be collected:** Blood samples for measuring serum Homocysteine levels.

Intervention

- No intervention involved.

Sampling design: Convenient sampling.

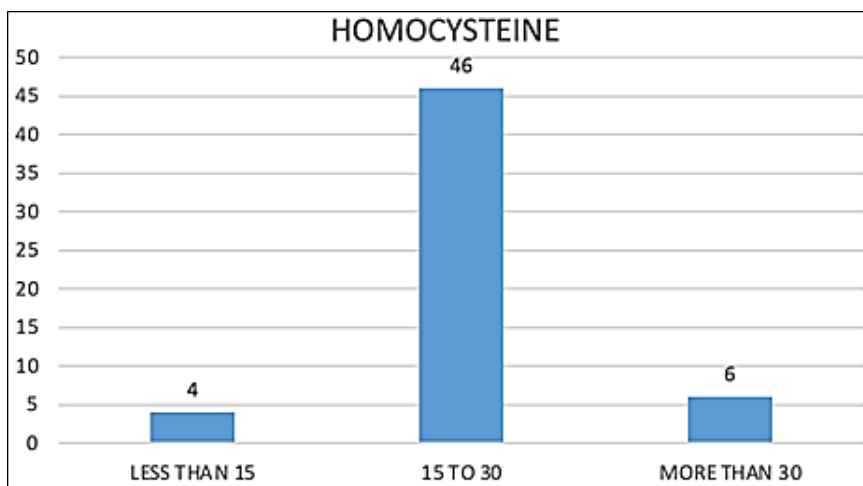
Statistical analysis

- Descriptive statistics and assessment of correlation coefficient between serum homocysteine and deep vein thrombosis.

Results

Table 1: Homocystenien Levels

Homocysteine Levels	Case Number	Percent of cases
Less Than 15	4	7.14%
15 to 30	46	82.14%
More Than 30	6	10.71%

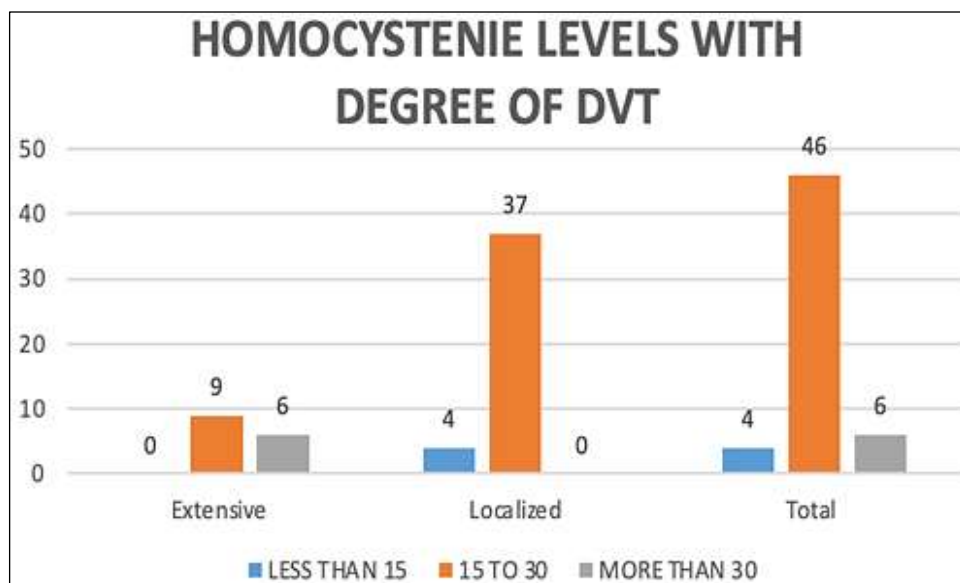


Graph 1: Homocystenien Levels

In the study in 7.14% had homocystenien levels below the normal limit of 15 units, 82.14% had normal levels and 10.71% had more than 25 units, all of them had extensive DVT.

Table 2: Homocystenien levels with degree of DVT

Homcysteine Levels	Extensive	Localized	Total	Extensive	Localized	Total
Less Than 15	0	4	4	0.00%	9.76%	7.14%
15 To 30	9	37	46	4.00%	90.24%	82.14%
More Than 30	6	0	6	40.00%	0.00%	10.71%
Total	15	41	56	100.00%	100.00%	100.00%



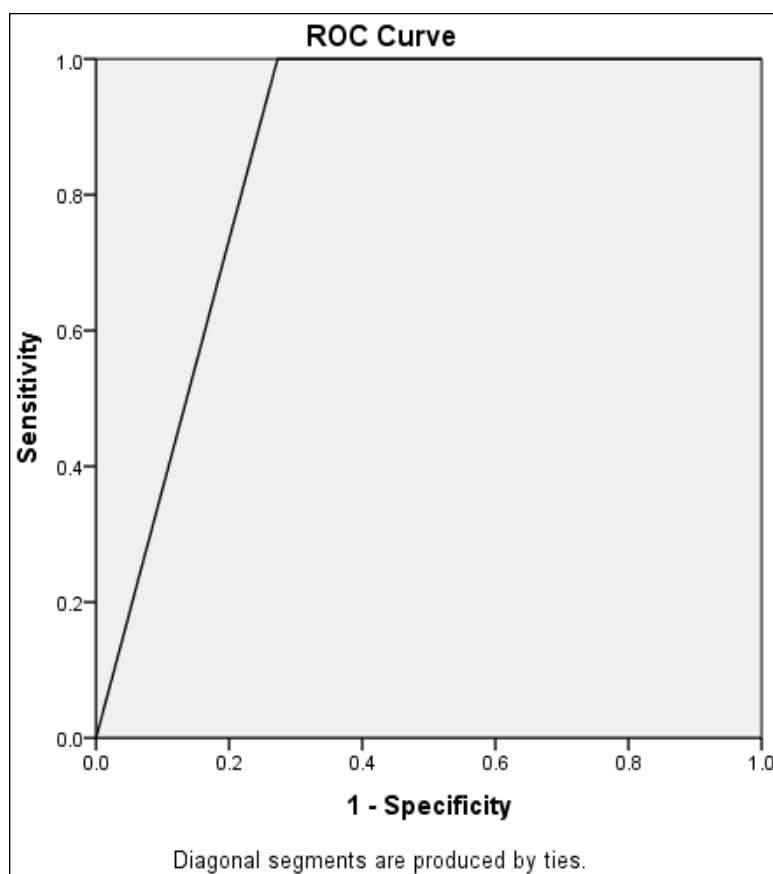
Graph 2: Homocystenien levels with degree of DVT

90.24% with extensive DVT had a homocystenien levels more than 25 units.

Area under curve of homocystenien levels

Table 3: Sensitivity of Homocystenien Levels

Statistic	Value	95% CI
Sensitivity	95.74%	85.46% to 99.48%
Specificity	70.00%	61.26% to 98.74%
Disease prevalence (*)	95.92%	86.02% to 99.50%
Positive Predictive Value (*)	97.83%	91.83% to 99.45%
Negative Predictive Value (*)	53.33%	46.71% to 77.66%
Accuracy (*)	93.88%	83.13% to 98.72%



Graph 3: Area under Curve of Homocysteinie Levels

ROC Curve-Area Under the Curve 0.864

The Sensitivity of 95.74%, Specificity of 70.00%, Disease prevalence of 95.92%, Positive Predictive Value of 97.83%, Negative Predictive Value of 53.33% and Accuracy of 93.88% at a cut off of 15 units.

Discussion

Serum level of homocysteine was higher in males

Ravari *et al.* ^[6] observed that there was a significant elevation in the serum concentration of homocysteine among males ($p < 0.01$). The prevalence of deep vein thrombosis (DVT) was much greater among males, with a male-to-female ratio of 2:1. The observed discrepancy in our investigation was found to be statistically significant, with a p-value of 0.002. This finding aligns with the results reported by Ravari *et al.* ^[6].

Number of cases serum homocysteine

Ravari *et al.* ^[6] observed that individuals with deep vein thrombosis (DVT) had a higher serum concentration of homocysteine compared to those without the condition, with percentages of 36% and 15% respectively. This difference was shown to be statistically significant, with a p-value of less than 0.01.

In a study conducted by Amparo Vayá *et al.* ^[8], it was seen that individuals with deep vein thrombosis (DVT) had higher blood levels of homocysteine compared to those without the condition. Specifically, the prevalence of elevated homocysteine levels was found to be 25% in the DVT group, while it was 11.5% in the non-DVT group. This difference was shown to be statistically significant, with a p-value of less than 0.01.

In a study conducted by Gautam V. Kamat *et al.* ^[7], it was observed that the prevalence of hyperhomocysteinemia among patients with deep vein thrombosis (DVT) was determined to be 31.428%.

The current study found that 92.86% of participants exhibited elevated levels of deep vein thrombosis (DVT). The patients were not assessed for the presence of atherosclerosis, which may have had an impact on the elevated levels of homocysteine.

Mean serum level of homocysteine

According to the study conducted by Mounira Amrane et colleagues ^[9], individuals diagnosed with deep vein thrombosis (DVT) had a mean blood level of homocysteine at $12.62 \pm 8.7 \mu\text{mol/L}$.

In a study conducted by Ritvik D Jaykar *et al.* ^[10], it was shown that individuals with deep vein

thrombosis (DVT) had a mean blood level of homocysteine at $15.12 \pm 5.47 \mu\text{mol/L}$.

It was observed that individuals aged 50 and above, when combined with another risk factor, exhibited a significantly increased likelihood of developing deep vein thrombosis (DVT). Specifically, individuals aged 60 years or older had an odds ratio of 2.95 for developing DVT. Obesity was associated with an odds ratio of 1.45, recent surgery with an odds ratio of 0.81, major trauma with an odds ratio of 0.41, acute medical illness with an odds ratio of 1.97, stroke with an odds ratio of 1.12, recent myocardial infarction or acute heart failure with an odds ratio of 0.23, past history of DVT or clot with an odds ratio of 0.23, central venous catheter with an odds ratio of 0.41, lower segment caesarean section with an odds ratio of 0.23 and cancer with an odds ratio of 1.97 for developing DVT.

The diagnostic test demonstrated a sensitivity of 95.74%, indicating its ability to correctly identify individuals with the disease. The specificity of the test was 70.00%, indicating its ability to correctly identify individuals without the disease. The disease prevalence was found to be 95.92%, representing the proportion of individuals in the population who have the disease. The positive predictive value of the test was determined to be 97.83%, indicating the probability that a positive test result accurately indicates the presence of the disease. Conversely, the negative predictive value was found to be 53.33%, representing the probability that a negative test result accurately indicates the absence of the disease. The overall accuracy of the test was calculated to be 93.88%, indicating the proportion of correct classifications made by the test. This accuracy was determined at a cut-off value of 15 units. Additionally, the area under the curve (AUC) was found to be 0.864, which provides a measure of the test's overall discriminatory ability.

Conclusion

It was shown that the levels of homocysteine were elevated in all individuals who had deep vein thrombosis (DVT). A positive linear relationship was seen between the severity of deep vein thrombosis and the levels of homocysteine. The degrees of involvement were much greater when the veins in the thigh were affected, in comparison to cases where only the veins in the calf were affected. It was also shown that there was a positive correlation between elevated levels of Homocysteine, namely at or above 25 units, and a history of previous clot formation, with a corresponding rise in the incidence of Deep Vein Thrombosis (DVT) episodes.

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