# PREVALENCE OF HYPERHOMOCYSTENEMIA IN DEEP VEIN THROMBOSIS

**By**

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Dissertation submitted to

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In partial fulfillment of the requirements for the degree of

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**IN**

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**Under the guidance of**

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**Dr. Harikrishnan Nair**

## LIST OF ABBREVATIONS

| | | |
|---|---|---|
| Cm | - | Centimeter |
| CT | - | Computed Tomography |
| DM | - | Diabetes Mellitus |
| DNA | - | Deoxy ribose nucleic Acid |
| DVT | - | Deep Vein Thrombosis |
| ELISA | - | Enzyme Linked Immuno Sorbent Assay |
| Hcy | - | Homocysteine |
| HTN | - | Hypertension |
| ICU | - | Intensive Care Unit |
| IHD | - | Ischaemic Heart Disease |
| IPG | - | Impedance Plethysmography |
| IVC | - | Inferior Vena Cava |
| LMWH | - | Low Molecular Weight Heparin |
| MRI | - | Magnetic Resonance Imaging |
| MRV | - | Magnetic Resonanace Venography |
| PAI –I | - | Plasminogen Activator Inhibitor 1 |
| PE | - | Pulmonary Embolism |
| UFH | - | Un-Fractionated Heparin |
| VTE | - | Venous Thromboembolism |

# ABSTRACT

**Background** : Hyperhomocystenemia is a known risk factor for the development of deep vein thrombosis. According various studies conducted in western countries, the prevalence of hyperhomocystenemia in patients with DVT varies from 10-25%. According to some studies, the prevalence of hyperhomocystenemia is higher in the Indian population. Hence the aim of this study was to determine the prevalence of hyperhomocystenemia in cases of DVT in our population and also to statistically analyse association of hyperhomocystenemia with risk factors like age, sex, Diabetes mellitus, hypertension, smoking, ischaemic heart disease, immobilization and anaemia.

**Objective** : To estimate the prevalence of hyperhomocystenemia in cases of Deep Vein Thrombosis and to statistically analyse association of hyperhomocystenemia with risk factors like age, sex, Diabetes mellitus, hypertension, smoking, ischaemic heart disease, immobilization and anaemia.

**Design** : Prospective cross sectional study

**Materials and Methods** : A total of 50 patients were included in the study. DVT was confirmed by doppler examination. Serum homocysteine was measured and the data was analysed. Statistical significance was calculated using Chi-square test.

**Results** : A total of 50 patients were studied. The prevalence of hyperhomocystenemia in cases of deep vein thrombosis in our population was 600 per

thousand cases. There was a statistically significant association between hyperhomocystenemia and immobilization, smoking and anemia.

**Conclusion** : The prevalence of hyperhomocystenemia in cases of deep vein thrombosis in our population was 600 per thousand cases. There was a statistically significant association between hyperhomocystenemia and immobilization, smoking and anemia . There was no association between hyperhomocystenemia and age, gender, IHD, HTN, DM and obesity in our study.

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# INTRODUCTION

Deep Vein Thrombosis (DVT) is a common but elusive illness that can result in suffering and death if not recognized and treated early. The venous thrombi can break off and form pulmonary emboli, obstructing the arteries of the lung and causing death. Though DVT and pulmonary embolism (PE) usually complicate the course of sick and hospitalized patients, they may also affect ambulatory and otherwise healthy persons.

Since venous thrombosis is difficult to recognize clinically, these hospitalized cases probably represent the tip of the iceberg. Unfortunately, the death rate from PE and DVT is substantial, and the probability of survival in affected is decreased when compared with unaffected ones.

The association between the risk for thromboembolism and a hypercoagulable state has been well known. Recent advances thrombosis research and laboratory medicine have provided an ever expanding list of specific laboratory anomalies that may predispose people to venous thromboembolism.

Mild Hyperhomocysteinemia is an established risk factor for atherosclerosis and vascular disease.[1,2] In classic homocystinuria, half the vascular complications are of venous origin,[3] but until recently it has been unclear whether mild Hyperhomocysteinemia is also a risk factor for venous thrombosis.[2,4,5]

In a case-control study, Falcon et al. found that Hyperhomocysteinemia was a risk factor for thrombosis in people younger than 40 years of age.[6] Recently, Hyperhomocysteinemia was found to be a risk factor for recurrent venous thrombosis

in patients between 20 and 70 years of age, as compared with controls from the general population.[7] Although the results of these studies support the hypothesis that mild Hyperhomocysteinemia is a risk factor for venous thrombosis, the studies were not designed to estimate the risk in general population.

Although, studies are available which gives us the prevalence of Hyperhomocysteinemia in patients with Deep Vein Thrombosis in the western population, no studies are mentioned in literature regarding the prevalence of Hyperhomocysteinemia in patients with DVT in the Indian population.

Thus, the present study was undertaken to detect the prevalence of Hyperhomocysteinemia in patients with DVT coming to our hospital.

# AIMS AND OBJECTIVES

To determine the prevalence of Hyperhomocysteinemia in cases of Deep Vein Thrombosis in Shri B.M Patil Medical College Hospital, Bijapur and to statistically analyse the association of hyperhomocystenemia with risk factors like age, sex, Diabetes Mellitus, Hypertension, smoking, Ischaemic heart disease, immobilization and anaemia.

# REVIEW OF LITERATURE

## Historical background

Venous diseases of the lower limbs, as noted by Linton in 1953, are greatly influenced by the erect position of the human race, and impairment of return of venous blood to the heart against gravity contributes to the development of both acute venous thrombosis and chronic venous insufficiency. It was not until 1810 that Ferriar described a patient with phlegmasia alba dolens, but he still presumed that the condition was caused by lymphatic obstruction. The relationship between phlegmasia alba dolens and acute Deep Vein Thrombosis (DVT) was established by Davis in 1822; he also recognized the relationship between venous thrombosis and childbirth. Virchow described his revolutionary discovery of the three main causes of DVT—changes in the venous wall, stasis of venous blood, and changes in the blood coagulation—in his book *Die Cellular Pathologie*. He recognized the association between Deep Vein Thrombosis and Pulmonary Embolism.[8]Surgical treatment of DVT at the end of the 19th century consisted of proximal ligation of the great saphenous vein, as described by Trendelenburg in 1891. In the early 20th century, stripping of the saphenous veins was added to proximal ligation. Reconstructive venous surgery dates back to 1877, when Eck first performed anastomoses between the portal vein and the inferior vena cava; in 1906, Carrel and Guthrie described their first attempts at venous anastomoses. John Homans, in 1917, introduced the terms venous stasis and post-thrombotic syndrome and classified varicose veins as primary and post-thrombotic. Bauer performed phlebographies regularly in patients to study DVT. The fibrinolytic effect of Streptococcus was first described in 1933 by Tillett and Garner, and heparin was first used successfully in humans. Bauer also showed the

beneficial effect of heparin on DVT in 1941. Research by Tillett and associates on the beneficial effect of streptokinase in venous thrombosis, published in 1955, started the era of thrombolysis in the management of acute venous thromboembolism.

**Epidemiology**

The exact incidence of DVT is not known due to the silent nature as well as non specific signs and symptoms of the disease. Autopsy studies reveal the prevalence to range between 35% to 52%. Community-based studies of venographically documented symptomatic DVT have reported a yearly incidence of 1.6 per 1000 residents. Among men, the cumulative probability of suffering a thromboembolic event is estimated to be 10.7% by the age of 80 years. Epidemiologic data from the Olmsted County project in Minnesota found that the overall average age- and sex-adjusted annual incidence of venous thromboembolism (VTE) was 117 per 100,000 (DVT, 48 per 100,000; PE, 69 per 100,000), with higher age-adjusted rates among men than women (130 vs. 110 per 100,000, respectively). One out of every 9 persons develops recognized DVT when younger than 80 years, and clinically recognized VTE (venous thromboembolism) accounts for 1 of every 20 deaths in those older than 50 years.[9] Autopsy studies demonstrate that approximately 80% of all cases of DVT and PE remain undiagnosed, even when they are the immediate cause of death. Therefore the true prevalence is unknown.

## The Physiology of Hemostasis, Coagulation, Anti Coagulation and Fibrinolysis

### Hemostasis

Platelet adhesion is the initiating event in venous thrombosis. Platelet adhesion and aggregation are stimulated by a substance known as electron- dense substance which is present in endothelial cells. This is exposed during endothelial cell injury. The release of this substance is enhanced by the activity of intrinsic coagulation cascade and is inhibited by platelet anti aggregating agents, thrombolytics and anticoagulants.

Activation of platelet causes the release of platelet proaggregants Thromboxane A2 and serotonin. This results in recruitment of more platelets to form a haemostatic plug. Thromboxane A2 and serotonin also bring about local vasoconstriction. Exposure of the platelet membrane phospholipids catalyze activation of Factor X and local formation of thrombin which itself act as powerful procoagulant.

### Coagulation

Activation of coagulation pathways and thrombin generation occurs once the haemostatic plug is well established. It is initially a loose aggregation of blood elements. Fibrin cross linkages are established which helps in the formation of a true thrombus. There are however three factors that help in preventing uncontrolled formation and propagation of thrombus:

- Flow dilution
- Natural anticoagulants
- Natural thrombolytics

## Anticoagulation

Protein C, Protein S and anti thrombin III are some of the best known circulating natural anticoagulants. Antithrombin III is an inhibitor of the intrinsic pathway. Protein C inhibits factor V and factor VIII, which are mainly involved in the common pathway.

Other plasma proteins serve as activators, inhibitors, or cofactors in the coagulation cascade. These include proteases such as heparin cofactor II, alpha 2 macroglobulin, alpha 1 antitrypsin and C1 inhibitor. For example, the isolated deficiency of heparin co factor II can cause recurrent venous thrombosis, and that of other co factors can increase the likelihood of thrombosis in response to vascular injury or venous stasis. Together, these plasma proteins prevent minor endothelial injury from initiating uncontrolled intravascular coagulation.

## Fibrinolysis

Fibrinolysis is a process of fragmentation of fibrin and fibrinogen and protects against the formation of thrombus. It is initiated by tissue activators and by the circulating activators that convert inactive plasminogen into plasmin, the active fibrinolytic agent. Plasmin attacks and degrades fibrin, when excess plasmin is present; it also attacks and degrades fibrinogen. Damage to the endothelial cells causes platelet adhesion and initiation of the clotting mechanism. At the same time, it also causes release of tissue plasminogen activator (t-PA). A delicate balance is ensured under normal conditions, so that the formation of thrombus is localized to the injury site. Any disturbance in this delicate balance leads either to increased propagation of thrombi or bleeding.

Impaired fibrinolytic activity permits thrombus propagation and leads to an increased likelihood of clinically apparent venous thrombosis.

**Etiology**

All recognized risk factors for DVT arise from 3 underlying components of the Virchow's triad :[8]

- Venous Stasis
- Hypercoagulability
- Endothelial injury

It also clear, however, that the origin of DVT is frequently multifactorial, with components of Virchow's triad assuming variable importance in individual patients. The single most important risk factor for DVT is prior history of VTE. Patients who have had prior DVT or PE have high chances of developing recurrent VTE with surgery.

Mechanical venous injury clearly plays a role in thrombosis associated with direct venous trauma, hip arthroplasty, and central venous catheters. Central venous cannulation is largely responsible for the increasing incidence of upper extremity thrombosis, whereas similar venous injury is presumably responsible for the observation that 57% of thrombi occurring after hip arthroplasty arise from the femoral vein rather than the usual site in the calf. Focal venous injury cannot account for the observations that thromboses in trauma patients are more commonly bilateral (77%) than unilateral (23%) and may be as common in an injured limb as in an

uninjured limb. Neither do mechanical crush injuries in animal models usually cause thrombosis, even when followed by stasis. Overt endothelial injury likely is neither necessary nor sufficient to cause thrombosis in the absence of other stimuli.

The potential role of biochemical injury to the venous endothelium has only lately become apparent. The normal venous endothelium is antithrombotic, producing prostaglandin I2 (PGI2, prostacyclin), glycosaminoglycan cofactors of antithrombin, thrombomodulin, and tissue-type plasminogen activator (t-PA). However, the endothelium may become prothrombotic under some conditions, producing tissue factor, von Willebrand factor, and fibronectin. It is conceivable that some thrombotic risk factors act through production of a procoagulant endothelium. Microscopic changes in the endothelial surface associated with greater endothelial permeability and leukocyte adhesion have been demonstrated in response to distant surgical injury. Induction of procoagulant activity, suppression of anticoagulant mechanisms, and exposure of neutrophil receptor ligands may accompany such endothelial perturbation.

The importance of cytokine-mediated expression of tissue factor procoagulant activity under clinical conditions is unknown, but both interleukin-1 (IL-1) and tumor necrosis factor (TNF) may induce fibrin deposition through a combination of endothelial procoagulant expression and fibrinolytic depression. TNF also may downregulate endothelial thrombomodulin expression, further converting the endothelium from an antithrombotic to a procoagulant state. Virchow’s concept of venous injury may be more important at the molecular than the macroscopic level.

Regardless of etiology, most venous thrombi originate in areas of low blood flow, either in the soleal veins of the calf or behind valve pockets. Furthermore, many risk factors for acute DVT are associated with immobilization and slow venous flow, and several mechanisms have been advanced to explain the role of stasis in thrombogenesis. In comparison with pulsatile flow, static streamline flow is associated with profound hypoxia at the depths of the venous valve cusps and may induce endothelial injury. The effects of hypoxia in cultured endothelial cells have been noted to include stimulation of cytokine production and leukocyte adhesion molecule expression, perhaps accounting for the adhesion and migration of leukocytes observed in association with stasis. Furthermore, stasis also allows the accumulation of activated coagulation factors and the consumption of inhibitors at sites prone to thrombosis. Stasis in the large veins may be particularly important, because the low surface-to-volume ratio may prevent interaction with endothelial inhibitory pathways, particularly the endothelium-bound thrombomodulin– protein C system. Despite these observations, there is little evidence that stasis can activate coagulation, and in isolation, stasis appears to be an inadequate stimulus for thrombosis.

Activation of coagulation appears to be critical in the pathogenesis of DVT. The coagulation cascade functions through serial activation of zymogens in the intrinsic and tissue factor pathways, with the ultimate generation of thrombin by the prothrombinase complex. Antithrombin and the Thrombomodulin–Protein C systems are the primary inhibitors of coagulation, whereas the fibrinolytic system serves to further limit fibrin deposition. Although the hemostatic system is continuously active, thrombus formation is ordinarily confined to sites of local injury by a precise balance between activators and inhibitors of coagulation and fibrinolysis. A prothrombotic

state may result either from imbalances in the regulatory and inhibitory systems or from activation exceeding antithrombotic capacity.

Identification of activated coagulation has been facilitated by the development of sensitive assays for stable byproducts of thrombin activation. The most useful of these byproducts are:

- Prothrombin fragment F1+2 , generated by factor Xa in the cleavage of prothrombin to thrombin
- Fibrinopeptide A, formed in the thrombin-mediated conversion of fibrinogen to fibrin
- Thrombin-antithrombin complex, formed by the combination of thrombin with its primary inhibitor

Increased levels of these markers have been described in association with risk factors such as surgery, oral contraceptives, and malignancy. Just as the combination of stasis and injury may be ineffective in causing thrombosis without low levels of activated coagulation factors, activated coagulation alone may be insufficient to provoke thrombosis. Ordinarily, activated coagulation factors are rapidly cleared from the circulation. When localized in regions of stasis, however, the coagulation cascade allows activated factors to rapidly amplify the thrombotic stimulus, leading to platelet aggregation and fibrin formation. DVT thus appears to be a multifactorial phenomenon, with convergence of several pathologic factors often required to produce a thrombotic event.

**Risk factors for DVT[9,11]**

DVT occurring in the setting of a recognized risk factor is often defined as secondary, whereas that occurring in the absence of risk factors is termed primary or idiopathic.

1. **Age**

   VTE occurs in both the young and the elderly, although a higher incidence has consistently been associated with advanced age. Increasing age is an important risk factor for DVT and PE. In a community-based study of phlebographically documented DVT, the yearly incidence of DVT was noted to increase progressively from almost 0 in childhood to 7.65 cases per 1000 in men and 8.22 cases per 1000 in women older than 80 years. The incidence of DVT increased 30-fold from age 30 years to 80 or more years. The influence of age on the incidence of VTE is likely multifactorial. The number of thrombotic risk factors increases with age, three or more risk factors being present in only 3% of hospitalized patients younger than 40 years but in 30% of those 40 years and older. Advanced age also has been associated with anatomic changes in the soleal veins and with more pronounced stasis in the venous valve pockets.

   VTE in children is almost always associated with recognized thrombotic risk factors, and multiple risk factors are often required to precipitate thrombosis. Venous thrombosis is more common in some pediatric populations, such as children hospitalized in the intensive care unit, those with spinal cord injuries, and those undergoing prolonged orthopedic immobilization, although the incidence is substantially lower than in corresponding adult populations. Other

thrombotic risk factors noted in hospitalized children are local infection and trauma, immobilization, inherited hypercoagulable states, oral contraceptive use, lower limb paresis, and the use of femoral venous catheters.

2. **Anaesthesia**

Patients receiving general anesthesia have a 500% increased risk of DVT compared with patients receiving epidural anesthesia for the same surgical procedure.

3. **Autoimmune disease and immune deficiency**

9% patients with Systemic Lupus Erythematosus develop spontaneous DVT. Lupus anticoagulant is present in 34% of patients with SLE, and anticardiolipin antibodies in 44%, in comparison with 2% and 0% to 7.5%, respectively, in the general population. Among patients with SLE, those with lupus anticoagulant are at a six fold higher risk for VTE, whereas those with anticardiolipin antibodies are at a twofold greater risk. The incidence of arterial or venous thrombosis is 25% in patients with lupus anticoagulant and 28% in patients with anticardiolipin antibodies.

4. **Blood surface antigens**

Type A blood is associated with lower levels of Antithrombin III and higher levels of factor VIII than type O blood. In the reproductive age group, women with type A blood are 4 times as likely to develop DVT compared with women with type O blood.

## 5. Cancer

Malignancy has been identified as an important marker of DVT, and spontaneous DVT without an obvious cause may be secondary to an undiagnosed malignancy. A recognized malignancy is present in 19% to 30% of patients with DVT. An association between mucin-secreting gastrointestinal tumors and thrombosis has long been recognized. However, carcinoma of the lung is more prevalent and is now the most common tumor associated with VTE, accounting for one quarter of cases. DVT may also herald a previously undetected malignancy in 3% to 23% of patients with idiopathic thrombosis. The thrombogenic mechanisms associated with cancer may be heterogeneous, but likely they involve release of substances that directly or indirectly activate coagulation. Tissue factor and cancer procoagulant, a cysteine protease activator of factor X, are the primary tumor cell procoagulants; associated macrophages may also produce procoagulants as well as inflammatory cytokines. As many as 90% of patients with cancer have abnormal coagulation parameters, including increased levels of coagulation factors, elevated fibrinogen or fibrin degradation products, and thrombocytosis. Elevated fibrinogen values and thrombocytosis are the most common abnormalities, perhaps reflecting an overcompensated form of intravascular coagulation. Levels of the coagulation inhibitors antithrombin, protein C, and protein S also may be reduced in malignancy. Furthermore, these levels may fail to normalize after administration of heparin to patients with cancer and DVT, perhaps explaining why their DVT may be refractory to anticoagulants

6. **Strokes and neurotrauma**

   Stroke and neurological trauma including neurosurgery are important risk factors for DVT. Without prophylaxis, about half of the patients develop acute DVT within 5 days following a stroke. 40% of postoperative neurosurgical patients develop DVT.

7. **Chemotherapy**

   Many types of chemotherapy increase the risk of DVT and PE. VTE has been reported in up to 6% of patients undergoing treatment for non-Hodgkin's lymphoma, in 17.5% of those receiving therapy for breast cancer, and in patients being treated for germ cell tumors. Among patients with stage II breast cancer, thrombosis was significantly more common in those randomly assigned to 36 weeks of chemotherapy (8.8%) than in those receiving only 12 weeks of treatment (4.9%).

8. **Coagulopathy**

   Deficiencies of protein C, protein S, or antithrombin III are well recognised coagulopathies that together account for approximately 15% of the cases of DVT. Resistance to activated protein C accounts for more. The lupus anticoagulant is another common coagulopathy that can be inherited or acquired.

9. **Fibrinolysis**

   Impaired fibrinolysis occurs in several inherited syndromes. It is most common in postoperative patients, those on synthetic estrogens of any type, and women who are pregnant or postpartum.

**10. Heart diseases**

Acute myocardial infarction and congestive heart failure increase the likelihood of DVT and PE, independent of bed rest or immobilization. Patients with acute myocardial infarction who are not receiving anticoagulation have a 26-38% rate of DVT.

**11. Hyperlipidemia**

The presence of lipemic serum greatly increases the rapidity and extent of thrombus formation in response to vascular injury.

**12. Immobility**

Immobilization producing stasis of blood is the most important risk factor for DVT and PE. Stasis in the soleal veins and behind the valve cusps is exacerbated by advancing age and inactivity of the calf muscle pump, both of which are associated with an increased risk of DVT. The prevalence of lower extremity DVT in autopsy studies also parallels the duration of bed rest, with an increase during the first 3 days of confinement and a rapid rise to very high levels after 2 weeks. Preoperative immobilization is similarly associated with a twofold higher risk of postoperative DVT, and DVT among stroke patients is significantly more common in paralyzed or paretic extremities (53% of limbs) than in nonparalyzed limbs (7%). DVT occurs in 10% of all patients advised bed rest in a general medical ward and in 29% of those placed at bed rest in an intensive care unit.

**13. Inflammatory bowel disease**

Increased fibrinogen, factor VIII, and platelet activity and depressed levels of antithrombin III and alpha 2 macroglobulin is seen in patients with ulcerative colitis or crohn's disease. Hence these patients are at increased risk for DVT and PE.

**14. Hyperhomocystenemia**

The role of mild to moderate hyperhomocystenemia in the development of vascular disease has been documented and reviewed extensively.[12,13,14,15,16] Hyper-Hcy is associated with both venous[17] and arterial thrombosis[18], as opposed to thrombophilia defects. In a recent meta-analysis, including 9 published studies, Ray found that hyper-Hcy was a significant risk factor for venous thromboembolism (VTE)

**15. Obesity**

Obesity has long been accepted as a risk factor for DVT and PE, but the evidence supporting this association is not convincing.

**16. Oral Contraceptives and Hormonal Therapy**

Case-control and population-based studies have now established the use of oral contraceptives as an independent risk factor for the development of DVT. Case control and cohort studies suggest a relative risk of approximately 3-12 times higher for patients taking oral contraceptives compared with patients not taking them. The risk of hospital admission for a thromboembolic event, including cerebral thrombosis, has been estimated to be 0.4 to 0.6 per 1000 for

oral contraceptive users, compared with 0.05 to 0.06 for non-users. Risk is correspondingly higher when oral contraceptive use is combined with other factors, such as surgery and inherited inhibitor deficiencies.

Thromboembolic risk may be related both to the dose of estrogen and the type of progestin in contraceptive preparations. Preparations containing less than 30 to 50 μg of estrogen are associated with less thrombotic risk; the relative risks of intermediate-dose (50 μg of estrogen) and high-dose (>50 μg of estrogen) contraceptives is 1.5 and 1.7 times, respectively, than that of low-dose preparations (<50 μg of estrogen). Although no clear dose-response relationship has been demonstrated for progestin potency and DVT, third-generation contraceptives containing the progestin desogestrel, norgestimate, or gestodene have been associated with a twofold higher risk of VTE than second-generation drugs. The risk of VTE among users of third-generation oral contraceptives may be up to eight times that of young women who do not use oral contraceptives.

Estrogenic compounds also increase the risk of VTE when used for lactation suppression, in treatment of carcinoma of the prostate, and as postmenopausal replacement therapy. Although estrogen doses used for postmenopausal replacement therapy are approximately one sixth those in oral contraceptives, some data support an increased thromboembolic risk at these doses as well. Several studies have now reported a twofold to fourfold higher risk among women taking hormone replacement therapy. This increased risk is greatest during the first year of treatment.

Estrogen in pharmacologic doses is associated with alterations in the coagulation system that may contribute to this thrombotic tendency. Such alterations include decreases in PAI-1 and increases in blood viscosity, fibrinogen, plasma levels of factors VII and X, and platelet adhesion and aggregation. An associated prethrombotic state is implied by rises in markers of activated coagulation occurring in conjunction with elevations of circulating factor VIIa and decreases in antithrombin and protein S inhibitor activity. The extent to which antithrombin and protein S are depressed is significantly less with lower-estrogen preparations.

**17. Polycythemia and thrombocytosis**

The risk of venous and arterial thrombosis increases linearly with an increasing haematocrit value. Forty percent of deaths in patients with polycythemiavera are related to thrombosis, but only a third of these are related to venous thrombosis.

**18. Pregnancy and puerperium**

VTE complicates 0.1% to 0.7% of pregnancies. The frequency of VTE in young women has been noted to be higher than that in men, with half of first episodes in women younger than 40 years being associated with pregnancy. Although the absolute numbers may be small, thromboembolism during pregnancy and the puerperium is associated with higher rates of preterm delivery and perinatal mortality, whereas PE is second only to abortion as a cause of maternal mortality.

DVT in pregnancy has been attributed to an acquired prethrombotic state in combination with impaired venous outflow due to uterine compression; 81%

to 97% of documented thromboses have been isolated to the left leg. A variety of coagulation factors, including fibrinogen and factors II, VII, VIII, and X, are increased during pregnancy. Perhaps more important, protein S levels are decreased by 50% to 60% early during pregnancy, with free protein S levels comparable to those in hereditary heterozygous protein S deficiency. Fibrinolytic activity has also been reported to diminish during pregnancy. The risk of puerperal DVT also increases with maternal age, suppression of lactation, hypertension, and assisted delivery but not with the number of pregnancies.

**19. Prior DVT**

Patients with a previous episode of DVT are 5 times more prone to develop new DVT when compared with patients with no prior history of DVT. Past history of DVT increases the risk of new postoperative DVT from 26% to 68%. A past history of clinically apparent PE increases the risk of new postoperative DVT to nearly 100%.

**20. Surgery**

Even minimal venous endothelial injury can cause perioperative DVT. The rate of postoperative DVT in patients who do not receive effective prophylaxis is 70% after non elective hip surgery, 48% after elective orthopaedic surgery, and 12% after elective general surgery.

**21. Tissue antigens**

HLA antigens like Cw4, Cw5, and Cw6 are associated with an increased frequency of DVT and PE.

## Relevant Anatomy

### Peripheral venous system

The peripheral venous system functions both as a reservoir to hold extra blood and a conduit to return blood from the periphery to the heart and lungs. The correct functioning of the venous system depends on a complex series of valves and pumps that are individually frail and prone to malfunction, yet the system as a whole performs remarkably well under extremely adverse conditions.

Primary collecting veins of the lower extremity are passive thin walled reservoirs that are tremendously distensible. Outflow from collecting veins is via secondary conduit veins that have thicker walls and are less distensible. Most of these veins are subfascial and are surrounded by tissues that are dense and tightly bound. These subfascial veins belong to the deep venous system. The greater saphenous vein is a superficial vessel that nonetheless lies within a fascial sheath through most of its course from the groin to the ankle.

### Deep venous system

No matter what pathway is taken, all venous blood is eventually received by the deep venous system on its way back to the right atrium of the heart. Five major named branches to the deep venous system are found in most patients, 3 below the knee and 2 above the knee. To confuse the issue, the principal deep venous trunk of the leg is called the popliteal vein from below the knee until it passes upwards and anteriorly through the adductor canal in the distal thigh, then its name changes to the femoral vein for the remainder of its course in the thigh.

**Deep veins of the calf**

The lower leg has 3 groups of deep veins: the anterior tibial vein, draining the dorsum of the foot; the posterior tibial vein, draining the sole of the foot; and the peroneal vein draining the lateral aspect of foot. From the ankle, the anterior tibial vein passes upwards anterolateral to the interosseous membrane, the posterior tibial vein passes upward posteromedially beneath the medial edge of the tibia, and the peroneal vein passes upward posteriorly through the calf. In most patients, each one of these is actually a pair of veins flanking an artery of the same name. Just below the knee, the 4 anterior and posterior tibial veins join with the 2 peroneal veins to become the single large popliteal vein.

**Deep veins of the thigh**

The popliteal vein courses proximally behind the knee and then passes anteromedially in the distal thigh through the adductor canal, at which point its name changes to the femoral vein. In the proximal thigh, the femoral vein and the deep femoral vein unite to form the common femoral vein, which passes upwards above the groin crease to become the iliac vein.

**Above the thigh**

The external iliac vein is the continuation of the femoral vein as it passes upward behind the inguinal ligament. At the level of the sacroiliac joint, it unites with the hypogastric vein to form the common iliac vein. The left common iliac is longer than the right and more oblique in its course, passing behind the right common iliac artery. At the level of the fifth lumbar vertebra, the 2 common iliac veins come together at an acute angle to form the inferior vena cava.

**The calf-muscle pump**

The passage of blood upwards from the feet against gravity depends on a complex array of valves and pumps. Muscle pumps of the calf and thigh provide the motive force for venous return. The most important of these is called the calf-muscle pump, often referred to as the “peripheral heart”. Inflow to a segment of deep vein is through intake valves from perforating veins and from the deep vein segment below. Outflow is through an outflow valve to the deep vein segment above. Squeezing of the vein segment occurs when muscle contraction increases the pressure within a fascial compartment.

**Clinical features**

**Sex**

The male to female ratio is 1.2:1 .

**Age**

DVT usually affects individuals older than 40 years.

**History**

The signs and symptoms of DVT are related to the degree of obstruction, to venous outflow and the inflammation of the vessel wall. The bedside diagnosis of venous thrombosis is insensitive and inaccurate.

Many of the patients are asymptomatic but the history may include the following

- *Edema: principally* unilateral, is the most specific symptom. Massive oedema with cyanosis and ischaemia (phlegmasia cerulean dolens) is rare.

- *Leg pain :* occurs in 50% patients, however, this is entirely non specific. Pain can occur on dorsiflexion of the foot (Homan's sign).
- *Tenderness :* occurs in 75% of patients but is also found in 50% of patients without objectively confirmed DVT.
- Clinical signs and symptoms of PE as the primary manifestation occur in 10% of patients with confirmed DVT.
- Warmth or erythema of skin can be present over the area of thrombosis.

**Physical examination**

No single physical finding or combination of symptoms and signs is sufficiently accurate to establish the diagnosis of DVT. The following is a list outlining the most sensitive and specific physical findings in DVT.

- Edema, principally unilateral
- Tenderness is usually confined to the calf muscles or along the course of the deep veins in the medial thigh. Pain and/or tenderness away from these areas are not consistent with venous thrombosis and usually indicate another diagnosis.

**Venous distension and prominence of subcutaneous veins**

The presence of indurated, cordlike, tender, subcutaneous veins suggests superficial thrombophlebitis. About 40% of the patients with superficial thrombophlebitis without coexisting varicose veins and with no other obvious pathology have an associated DVT.

Patients with superficial thrombophlebitis extending to the saphenofemoral junction are also at higher risk for associated DVT.

**Fever**

Patients with DVT may have a fever, which is usually low grade.

**Phlegmasia cerulean dolens**

Patients with venous thrombosis may have variable discolouration of the lower extremity. The most common abnormal hue is reddish purple from venous engorgement and obstruction.

In rare cases, the leg is cyanotic due to extensive obstruction to iliofemoral vein. This ischaemic form of venous occlusion was originally described as phlegmasia cerulea dolens or painful blue inflammation. The leg is markedly oedematous, painful and cyanotic. Petechiaes are often present.

**Phlegmasia alba dolens**

It refers to painful white inflammation of the limb. It signifies massive iliofemoral venous thrombosis and associated arterial spasm. The affected limb is often pale with poor or even absent distal pulses.

Though this is often confused with acute arterial occlusion, but the presence of swelling, petechiae, and distended superficial veins point to this condition.

**Homans sign**

Pain in the calf muscles on forced dorsiflexion of the foot with the knee extended is called as Homans sign. However, this sign is non specific for DVT. It is present in less than one third of patients with confirmed DVT . This sign may also be positive in patients suffering from inflammatory condition of the limb without associated DVT.

**Wells clinical score for DVT[19] :**

| **Clinical Parameter Score** | **Score** |
|---|---|
| Active cancer (treatment ongoing, or within 6 months or palliative) | +1 |
| Paralysis or recent plaster immobilization of the lower extremities | +1 |
| Recently bedridden for > 3 d or major < 4 wk | +1 |
| Localized tenderness along the distribution of the deep venous system | +1 |
| Entire swelling | +1 |
| Calf swelling >3 cm compared with the asymptomatic leg | +1 |
| Pitting edema (greater in the symptomatic leg) | +1 |
| Previous DVT documented | +1 |
| Collateral superficial veins (nonvaricose) | +1 |
| Alternative diagnosis (as likely or greater than that of DVT) | +2 |

**Total of above score :**

| | |
|---|---|
| High probability | > 3 |
| Moderate probability | 1 or 2 |
| Low probability | < 0 |

**Lab Studies**

Recent interest has focused on the use of D-dimer in the diagnostic approach to DVT. D-dimer fibrin fragments are present in fresh fibrin clot and in fibrin degradation products of cross-linked fibrin. Monoclonal antibodies specific for the D-dimer fragment are used to differentiate fibrin-specific clot from non-cross-linked fibrin and from fibrinogen. These specific attributes of the D-dimer antibodies account for their high sensitivity for venous thromboembolism.

D-dimer levels remain elevated in DVT for about 7 days. Patients presenting late in the course, after clot organization and adherence have occurred, may have low levels of D-dimer. Similarly, patients with isolated calf vein DVT may have a small clot burden and low levels of D-dimer that are below the analytic cut-off value of the assay. This accounts for the reduced sensitivity of the D-dimer assay in the setting of confirmed DVT.

**D-dimer results should be used as follows :**

A negative D-dimer assay result rules out DVT in patients with low-to-moderate risk and a Wells DVT score less than 2.

All patients with a positive D-dimer assay result and all patients with a moderate-to-high risk of DVT require a diagnostic study.

Protein S, protein C, antithrombin III, factor V Leyden, prothrombin 20120A mutation, antiphospholipid antibodies and homocysteine levels can be measured.

Deficiencies of these factors or the presence of these abnormalities all produce a hypercougulable state. These are rare causes of DVT.

**Imaging Studies**

Because of the inherent inaccuracy of clinical diagnosis that is based on the history, the physical examination and the assessment of risk factors, D-dimer testing and a determination of pretest probability should be used to identify those patients who require further objective diagnostic testing.

Diagnosing DVT and committing patients to the risks of anticoagulation therapy without confirmatory objective testing is unacceptable.

**Duplex ultrasonography :**

Technological advances in ultrasonography have permitted the combination of real-time ultrasonographic imaging with Doppler flow studies (duplex ultrasonography). The major ultrasonographic criterion for detecting venous thrombosis is failure to compress the vascular lumen, presumably because of the presence of occluding thrombus. The absence of the normal phasic Doppler signals arising from the changes to venous flow provides indirect evidence of venous occlusion.

Duplex ultrasonography is also helpful to differentiate venous thrombosis from hematoma, Baker cyst, abscess and other causes of leg pain and edema.

The primary disadvantage of duplex ultrasonography is its inherent inaccuracy in the diagnosis of calf vein thrombosis.

**Impedance plethysmography**

In some countries, impedance plethysmography (IPG) has been the initial noninvasive diagnostic test of choice. This procedure is based on recording changes in blood volume of an extremity, which are directly related to venous outflow. In the setting of proximal vein thrombosis, venous outflow of the lower extremity is slowed and the blood volume or venous capacitance is increased. Standardized graphs are used to discriminate normal IPG study results from abnormal results.

**MRI**

MRI has increasingly been used for evaluation of suspected DVT. In limited studies, the accuracy approaches that of the criterion standard, contrast venography.

MRI is the diagnostic test of choice for suspected iliac vein or inferior vena caval thrombosis when CT venography is contraindicated or technically inadequate. In suspected calf vein thrombosis, MRI is more sensitive than any other noninvasive study. Expense, lack of general availability and technical issues limit it use. Although MRI is highly sensitive and relatively specific, the cost of the examination, the technical complexity, and the lack of general availability limit the use of MRV as a screening tool[20,21].

**CT venography**

With the introduction of multidetector CT technology, CT venography has been incorporated into CT angiographic studies of the chest as part of the diagnostic evaluation for suspected PE. CT venography of the lower extremities is performed after scanning of the chest has been completed. Studies in which indirect CTV was compared with venography showed 100% sensitivity and 96-97 % specificity[22].

In the Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) study reported by Stein et al, the addition of CT venography to CT angiography of the chest increased the diagnostic sensitivity for venous thromboembolic disease than CT angiography alone[23].

The primary utility of CT venography is for the diagnosis of ileofemoral DVT. The iliac veins cannot usually be visualized by ultrasonography and a different diagnostic modality must be used. Herein lies the value of CT venography where venous occlusion proximal to the inguinal ligament may be detected.

**Medical therapy:**

**Treatment of DVT by anticoagulation**

Anticoagulation has been the mainstay of therapy for DVT and PE since the initial introduction of heparin into clinical use in the 1930s. Rapid anticoagulation is essential because thrombus progression and recurrent embolization are 15 times higher in patients who do not receive adequate anticoagulation within the first 48 hours.

After initial anticoagulation with heparin, long-term anticoagulation is usually maintained with warfarin. Warfarin should never be started without prior heparinization because warfarin reduces the levels of anticoagulants before it reduces the levels of procoagulant proteins. This produces a hypercoagulable state during the first 5-7 days. If heparin is not given during this period of warfarin induction, many patients have worsening thrombosis.

Intravenous unfractionated heparin is gradually being replaced in modern practice by subcutaneous fractionated low molecular weight heparins. These newer agents offer much easier dosing, a wider therapeutic window, fewer bleeding complications and faster and more reliable results. Several different preparations are available but the various heparins are not equivalent and each requires a different dosing regimen.

**Treatment of DVT by fibrinolysis**

Fibrinolytic therapy has intrinsic appeal because it is intuitively obvious that it is preferable to remove an abnormal clot rather than to allow it to remain in place. Besides the obvious advantage of restoring a widely patent outflow channel, lysis of a thrombus has been demonstrated to preserve and restore normal venous valve structure and function if performed early enough in the course of the disease process.

The cumulative evidence suggests that compared with anticoagulation alone, lytic therapy for DVT produces more rapid clot resolution, more complete clot resolution, a marked reduction in late symptoms and reduced likelihood of recurrent DVT. By removing the clot before venous value injury occurs, fibrinolysis can

maintain and restore normal physiologic function of the venous system of the leg, when anticoagulation alone fails to do so in the vast majority of cases.

In 1997 a study by Konstantinides et al, which was a 719 patient multicenter registry study of patients with PE, showed a mortality rate of 11.1% for patients initially treated with heparin, compared with 4.7% for patients initially treated with fibrinolytic agents[24].

**Surgery for DVT**

Surgical therapy for DVT may be indicated when anticoagulant therapy is ineffective, unsafe, or contraindicated. The major surgical procedures for DVT are clot removal and partial interruption of the inferior vena cava to prevent PE.

The rationale for thrombectomy is to restore venous patency and valvular function. Thrtombectomy alone is not indicated because rethrombosis is frequent. Heparin therapy is a necessary adjunct. Thrombectomy is reserved for patients with massive ileofemoral vein thrombosis (phlegmasia cerulean dolens) with vascular compromise when thrombolysis is absolutely contraindicated.

**Compression stockings**

The post thrombotic syndrome affects approximately 50% of patients with DVT after 2 years. Elderly patients and patients with recurrent ipsilateral DVT have the highest risk. Below-the-knee elastic stockings assist the calf muscle pump and reduce venous hypertension and venous valvular reflux. This reduces leg edema, aids the microcirculation and prevents venous ischemia.

The regular use of graduated elastic compression stocking reduces the incidence of the postphlebitic syndrome by 50%.

**Ambulation**

Controversy exists regarding the role of ambulation in the therapy of DVT. The study by Partsch cited 2 small previous studies that demonstrated that the incidence of a new PE after initiation of anticoagulant therapy with a LMWH did not increase significantly in patients treated with early ambulation and compression. The authors concluded that early ambulation and compression is not associated with any significant risk of PE[25].

**Surgical therapy :**

Long-term results after DVT are better whenever venous patency and valve function can be established early and maintained. No matter what treatment modality is chosen, preservation of patency and of venous valve function are the strongest predictors of a good long-term outcome.

In many patients, fibrinolysis alone is highly effective and it has become the primary treatment of choice for many forms of venous and arterial thrombosis. Unfortunately when thrombosis is extensive, fibrinolysis alone may be inadequate to dissolve the volume of thrombus present.

Venous thrombectomy is a rarely used method of clot extraction that may improve the long-term outcome if it is successful in establishing and maintaining patency.

**Filters for DVT**

The idea of placing a barrier in the inferior vena to prevent PE from DVT was first suggested by Trousseau in 1868. In the mid 1900s before the adoption of anticoagulant therapy, DVT and PE were generally managed by laparotomy and vena caval ligation. The IVC filters are inserted transvenously under simple local anesthesia. The current benchmark standard is the Greenfield filter. Its design incorporates all the features of an ideal filter - maintain caval patency, trap emboli preserve prograde caval blood flow, avoid stasis and enhance thrombolysis of trapped emboli. The Greenfield filter achieves a long-term patency rate of 98% with only a 4% incidence of recurrent PE.

Generally accepted indications for filter placement are (1) severe hemorrhagic complication on anticoagulant therapy or other absolute contraindications to anticoagulation and (2) failure of anticoagulant therapy, such as new or recurrent venous thrombosis or PE, despite adequate anticoagulation. The use of vena caval filters has expanded to include primary venous thromboembolism prophylaxis in special patient populations at increased risk of VTE.

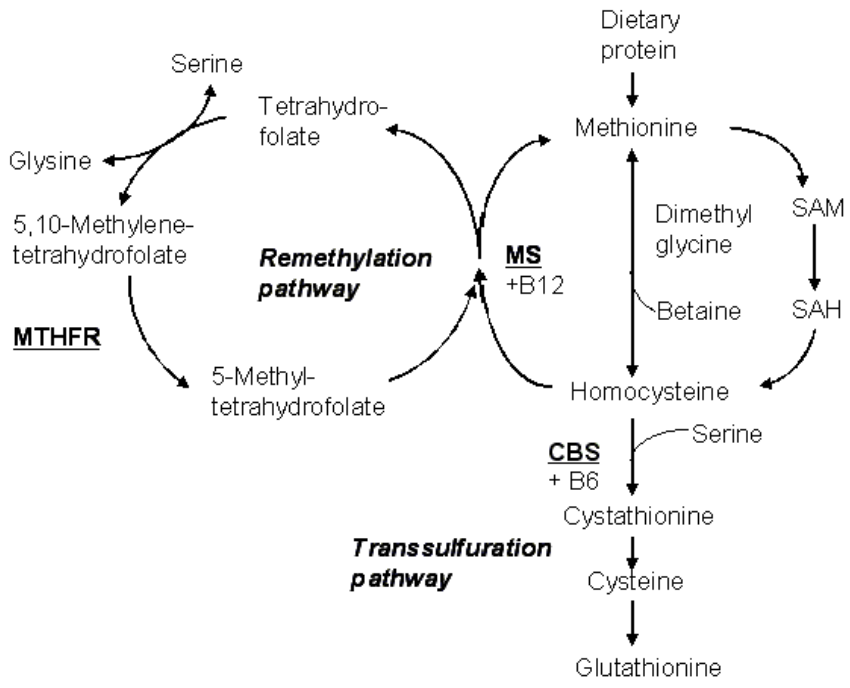
The study Decousus et al, randomized 400 patients with proximal DVT to filter groups. Both groups were anticoagulated with UFH. After 12 days, a statistically significant reduction occurred in PE in the filter group[26].

Currently, the newer filters are placed under ultrasonographic guidance either by transabdominal or by intravascular ultrasonography. The advantage of ultrasonography is that the filters may be placed at the bedside in the ICU or the ED, thereby avoiding the pitfalls and difficulties of transporting the patient to the angiography suite.

# HYPERHOMOCYSTEINEMIA

Homocysteine is a sulfhydryl containing amino acid derived from the essential amino acid methionine which is abundant in animal sources of protein[27]. The metabolic pathway that converts methionine to homocysteine is essential for the proper functioning of many biomolecules, including DNA, proteins, phospholipids and neurotransmitters [27,28,29].

In the methylation pathway, homocysteine acquires a methyl group either from betaine (a reaction that occurs mainly in the liver) or from 5-methylterahydrofolate (a reaction that occurs in all tissues and is vitamin B12-dependent). In the transsulfuration pathway, homocysteine is metabolized to cystathionine in a reaction catalysed by cystathionine-beta-synthase and required vitamin B6.



Plasma concentrations of homocysteine vary widely, but intracellular concerntrations of homocysteine are normally maintained within a relatively narrow range[29]. Total plasma (or total serum) homocysteine refers to the combined pool of free, bound, reduced and oxidized forms of homocysteine in the blood.

The following factors influence homocysteine metabolism and cause hyperhomocysteinaemia.

**Genetic factors**

1. 5, 10-Methylenetetrahydrofolate reductase C677T homozygosity (common)
2. Heterozygosity for cystathionine beta synthase defects (uncommon)
3. Homocystinuria (very rare)

**Physiological factors**

1. Increasing age
2. Male gender
3. Menopause
4. Reduced glomerular filtration rate
5. Increased muscle mass

**Lifestyle factors**

1. Reduced vitamin intake (folate, vitamin B12, vitamin B6)
2. Smoking
3. Caffeine consumption
4. Alcohol consumption
5. Physical inactivity

**Disease States**

1. Vitamin deficiency (folate, vitamin B12, vitamin B6)
2. Renal failure
3. Hypothyroidism
4. Diabetes mellitus
5. Psoriasis
6. Malignancies

**Drugs**

1. Lipid lowering –cholestyramine, nicotinic acid, fibric acid derivatives (eg, fenofibrate)
2. Anticonvulsants – phenytion, carbamazepine
3. Sex hormones – androgens
4. Other – cyclosporine, diuretics, levodopa methionine loading (oral, intravenous, peritoneal), theophylline, trimethoprim.

Many hypotheses have been proposed to explain how hyperhomocysteinemia may lead to venous thrombosis and atherosclerosis. One hypothesis is that homocysteine has a toxic effect on the vascular endothelium and on the clotting cascade[1,2]. However, virtually all these studies used amounts of homocysteine that produced higher than physiologic concentrations. Alternatively, hyperhomocysteinemia may reflect abnormal methionine metabolism that effects the methylation of DNA and cell membranes[30].

Causes of hyperhomocysteinemia are multifactorial[31,32]. Most operate by altering the function or blood concentrations of B vitamins (folic acid, vitamin B12, vitamin B6) involved as cofactors in the homocysteine metabolic pathway, interfering

with renal function, or influencing enzyme activities. The single most important determinant of tHcy in the general population is folate status[29].

Lowering plasma homocysteine concentrations by folic-acid-based vitamin supplementation is recommended in the treatment of hyperhomocysteinemia.

**Definition of Hyperhomocysteinemia**

An elevated plasma tHcy level (hyperhomocysteinemia) is most commonly defined according to arbitrary cut-off points (e.g. 95th percentile) in the distribution of values obtained from the so-called normal population. Each laboratory should establish reference limits for its own region, with separate reference limits for children, adults the elderly and pregnant women.

Laboratory studies suggest that an elevated tHcy level is both atherogenic and thrombogenic[27,33,34,35]. Given below are the proposed mechanisms by which hyperhomocysteinemia produces these complex changes in the structure and function of cerebral, coronary and peripheral vessels.

**Atherogenesis**

- Induces DNA hypomethylation and expression of genes known to mediate cell growth and differentiation.
- Induces oxidative stress.
- Induces vascular inflammation by altering expression of tumour necrosis factor –alpha and inducible Nitric Oxide synthase.

- Induces endothelial dysfunction as a result of increased oxidative stress, decreased bioavailability of nitric oxide (due to increased oxidative stress), and increased inflammation.
- Alters hepatic and macrophage lipoprotein metabolism, in part by enhancing uptake of modified low density lipoprotein.
- Induces hypertrophy and altered mechanics in the microcirculation, and increases intima media thickness.

**Thrombogensis**

- Induces tissue factor expression in monocytes.
- Modulates leukocyte-endothelium interactions.
- Increases platelet aggregation.
- Enhances binding of lipoprotein –A to fibrin.
- Interferes with several clotting factors.

Folic acid has been shown to prevent postprandial endothelial dysfunction in normohocysteinaemic subject and to improve endothelial function in patients with hyperhomocysteinemia, hypercholesterolemia, diabetes and coronary artery disease[29]. The exact mechanisms underlying the ameliorative effects of folate on the endothelium are uncertain, but may include homocysteine-lowering, antioxidant actions, effects on cofactor availability or direct interactions with the enzyme endothelial nitric oxide synthase[33,34,35].

# MATERIALS AND METHODS

**SOURCE OF DATA :**

All patients admitted in BLDEU'S SHRI B.M PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTER, BIJAPUR with symptoms of DVT confirmed by Doppler study during the period from September 2011 to June 2013 were selected for the study. The plasma homocysteine of all the subjects were estimated.

**SAMPLING:**

- Type of study – cross- sectional study
- Time period of study—September 2011 to June 2013.
- 50 patients were included in the study and their blood levels of homocysteine was estimated. With incidence rate of DVT 1 case per 1000 population i.e 0.1% , at 95% confidence interval and +/- 1 margin of error, the calculated sample size is 38 using the formula

  $N = \{(1 – 96)2 * p(1-p)\}/d2$

**INCLUSION CRITERIA :**

All diagnosed cases of DVT confirmed by doppler ultrasound with risk factors like

- Prolonged immobilization
- Smoking
- Anaemia
- Diabetes mellitus

- Hypertension
- Ischaemic heart disease
- Post menopausal state

**EXCLUSION CRITERIA:**

There was no exclusion criteria

**METHODOLOGY :**

- All cases of DVT confirmed by Doppler study were taken up for study. A detailed history was taken. Overnight fasting venous blood sample was collected from cubital vein in plain bulb and sent for serum homocysteine estimation.
- Estimation of serum homocysteine was done using photometry method.
- Reference Range :

  Adult Male : 6-15 mmol/L

  Adult Female : 3-12 mmol /L

  Elderly : 15-20 mmol/L

- Prevalence was calculated using the formula

$$\text{Prevalence} = \frac{\text{number of patients with DVT and homocystenemia}}{\text{The total number of patients with DVT}} \times 1000$$

- Statistical analysis for significance of difference between age, sex, and presence or absence of the risk factors such as DM, HTN, smoking, IHD, immobilization was done using the Chi square test.

# OBSERVATION AND RESULTS

A total of 50 patients with DVT were selected for the study. Of these 50 patients, 30 patients were found to have raised homocysteine levels. The prevalence of hyperhomocystenemia in cases of DVT in this study was calculated as 600 cases per thousand population. The same has been shown in the pie chart below-

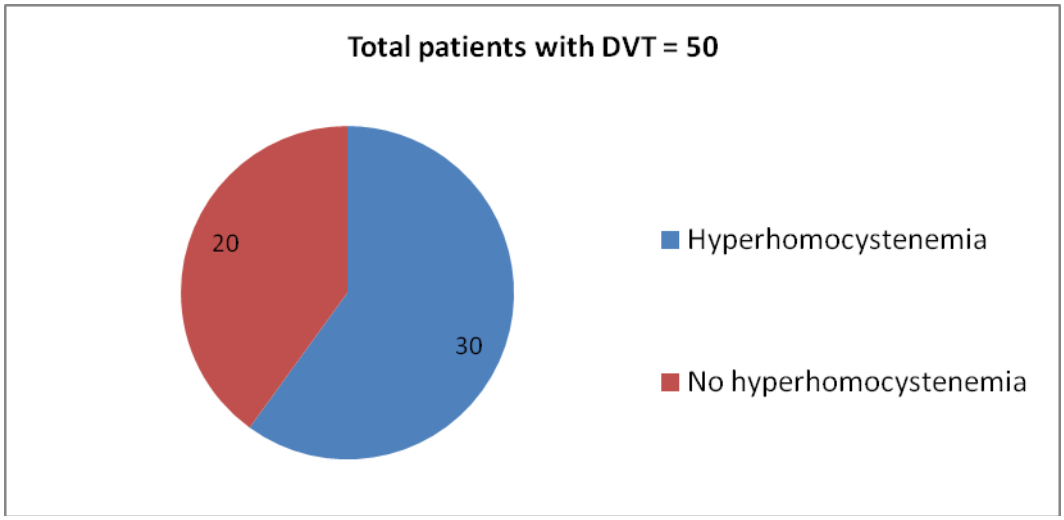


**Table No 1: Frequency & percentage distribution patients according to age**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Age in year** | **Absent** | **%** | **Present** | **%** | **Total** |
| 24-43 | 08 | 40.0 | 15 | 50.0 | 23 |
| 44-63 | 07 | 35.0 | 07 | 23.3 | 14 |
| 64-83 | 05 | 25.0 | 08 | 26.7 | 13 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph No1: Frequency & percentage distribution patients according to age**

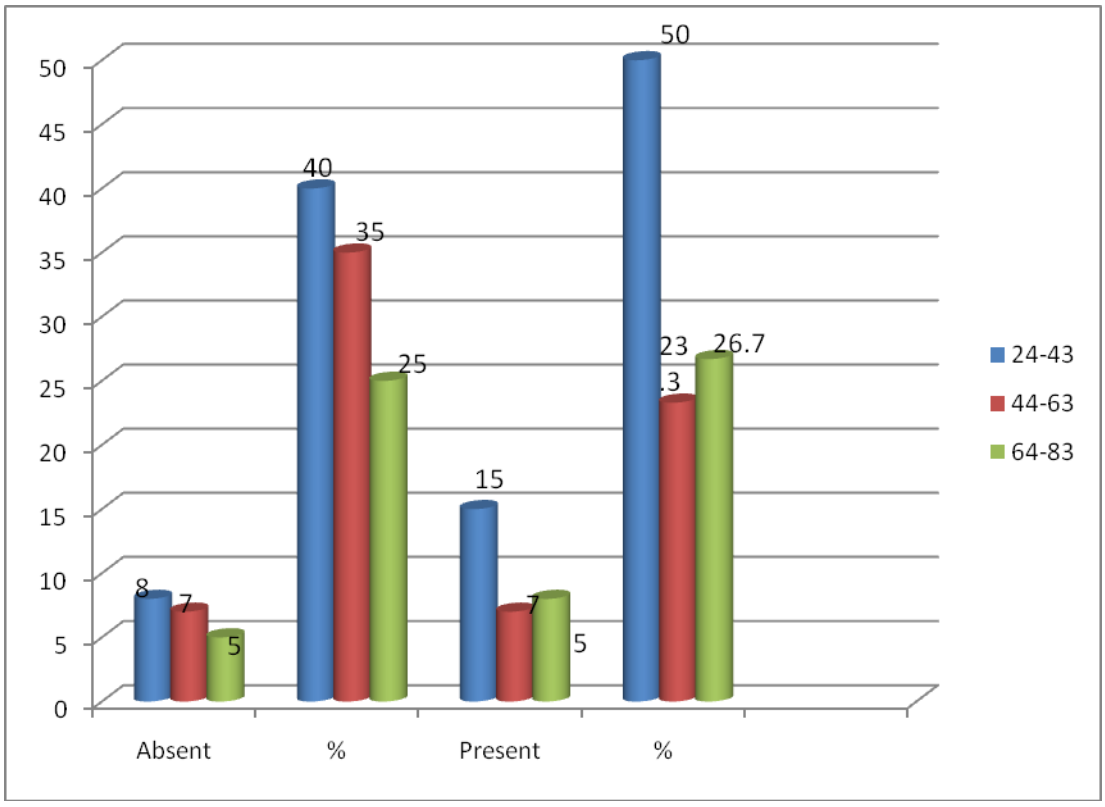


**Table No 2: Frequency & percentage distribution patients according to sex**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Sex** | **Absent** | **%** | **Present** | **%** | **Total** |
| Male | 11 | 55 | 14 | 46.7 | 25 |
| Female | 09 | 45 | 16 | 53.3 | 25 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph No2: Frequency distribution patients according to sex**

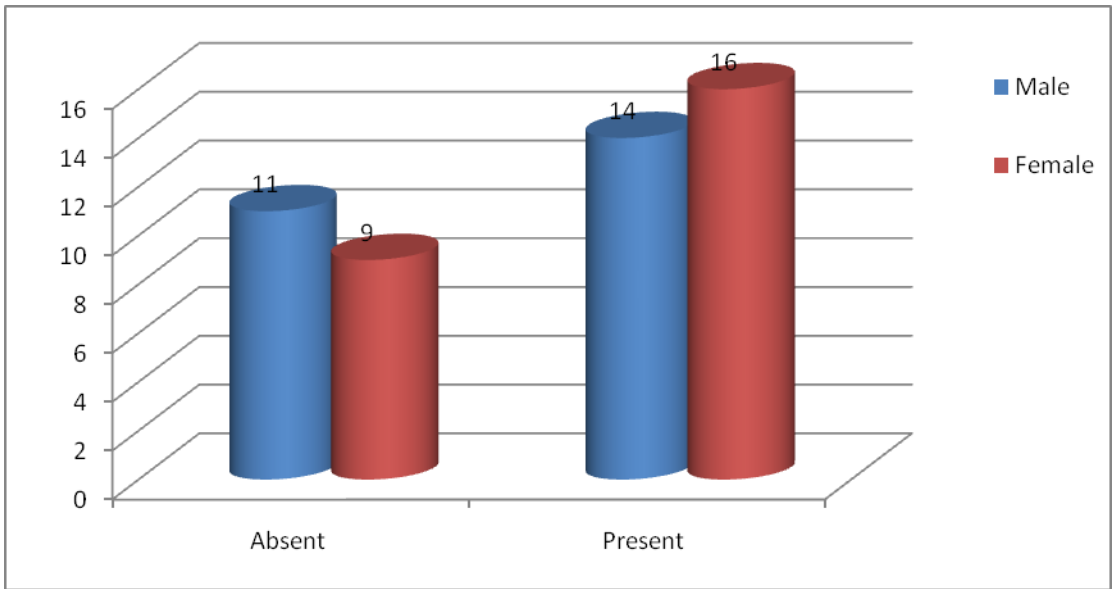


**Table No 3: Frequency & percentage distribution patients according to immobilization**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Immobilization** | **Absent** | **%** | **Present** | **%** | **Total** |
| Present | 04 | 20.0 | 18 | 60.0 | 22 |
| Absent | 16 | 80.0 | 12 | 40.0 | 28 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph 3: Frequency & percentage distribution patients according to immobilization.**

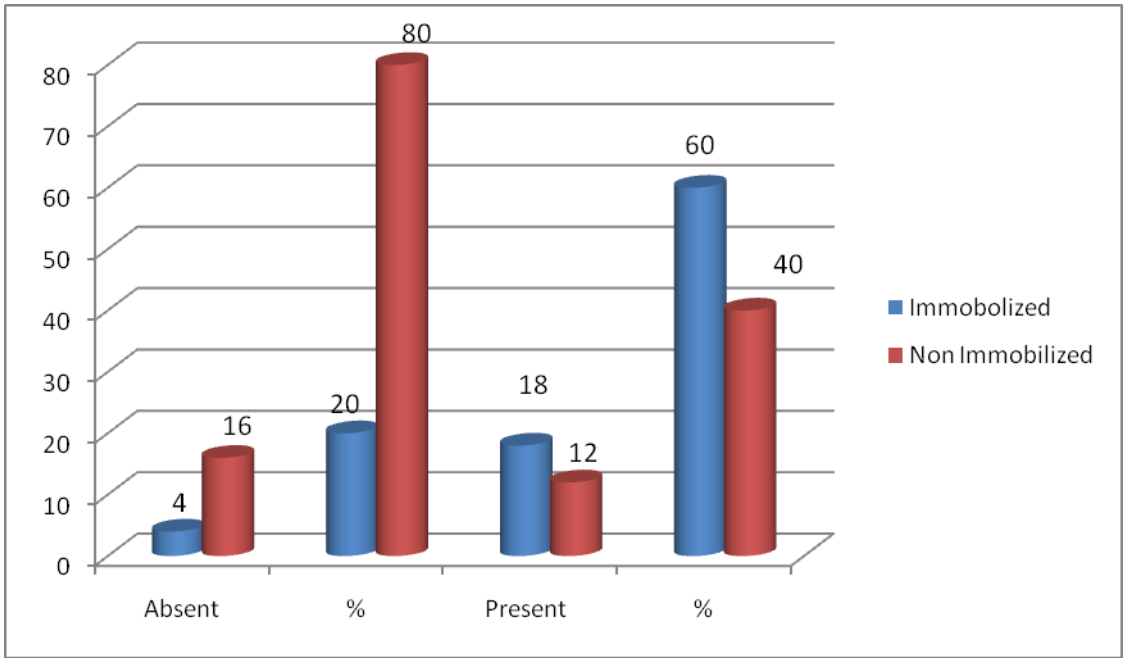


**Table No 4: Frequency & percentage distribution patients according to smoking/Tobacco chewing**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Smoking** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 13 | 65.0 | 09 | 30.0 | 22 |
| Present | 07 | 35.0 | 21 | 70.0 | 28 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph NO 4: Frequency & percentage distribution patients according to smoking/tobacco chewing**

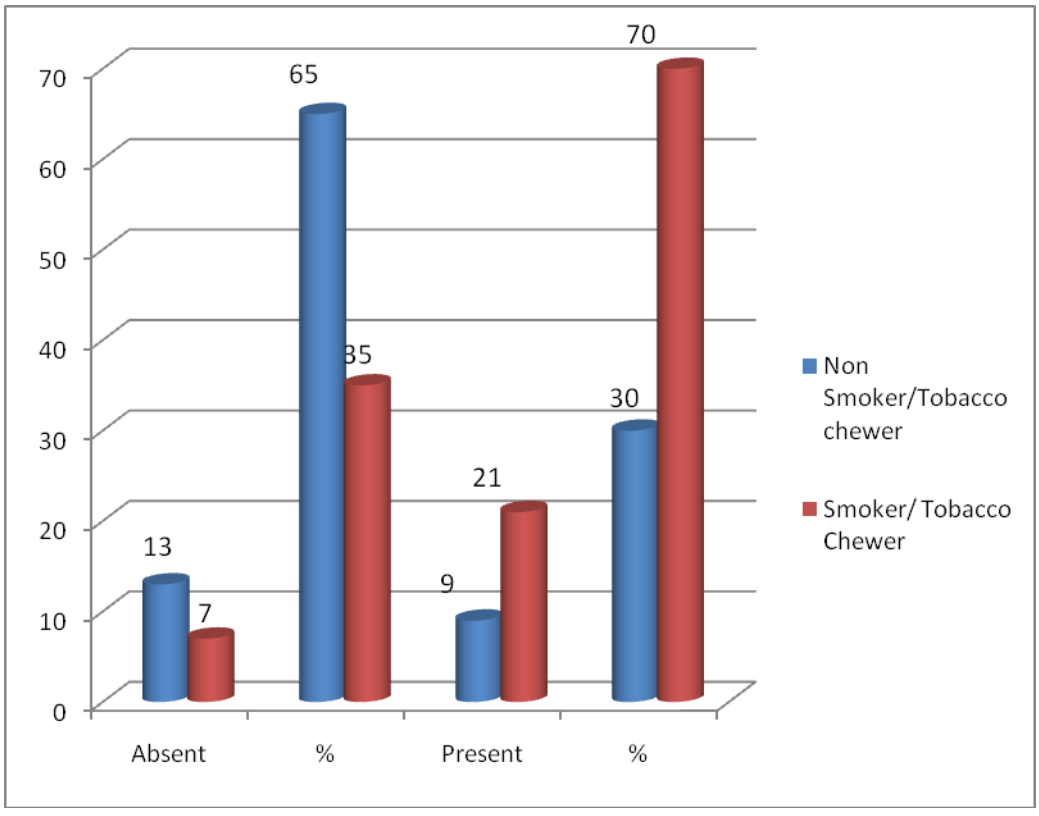


**Table No 5: Frequency & percentage distribution patients according to IHD**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **IHD** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 15 | 75.0 | 27 | 90.0 | 42 |
| Present | 05 | 25.0 | 03 | 10.0 | 08 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph NO 5: Frequency & percentage distribution patients according to IHD**

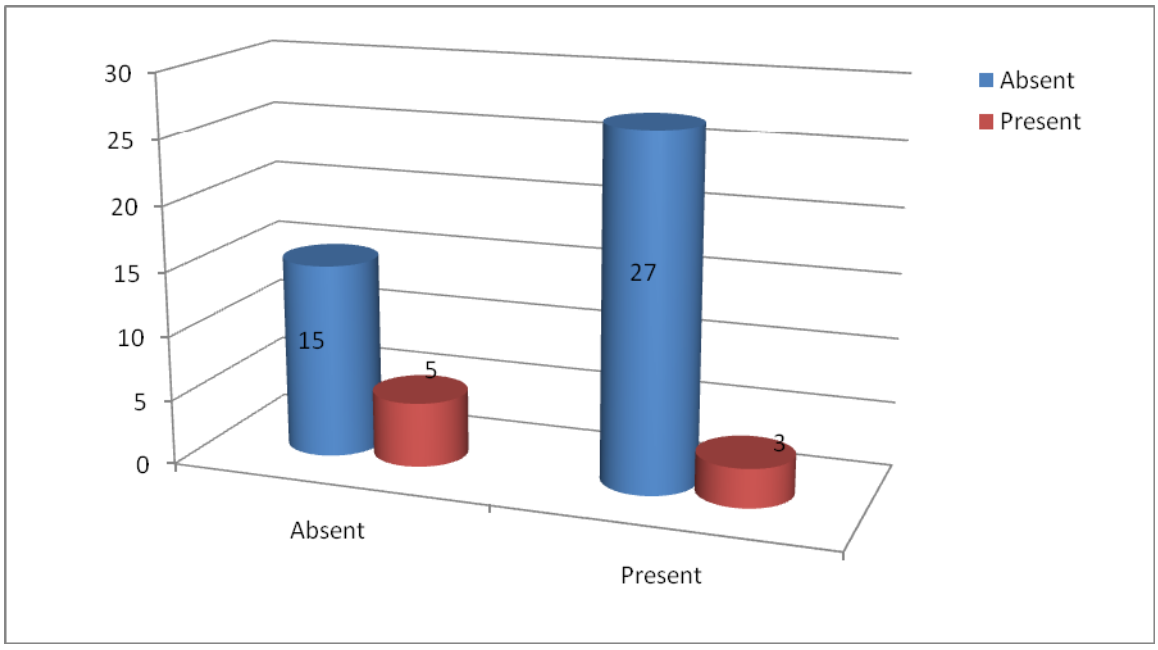


**Table No 6: Frequency & percentage distribution patients according to obesity**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Obesity** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 18 | 90.0 | 26 | 86.7 | 44 |
| Present | 02 | 10.0 | 04 | 13.3 | 06 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph No 6: Frequency & percentage distribution patients according to obesity**

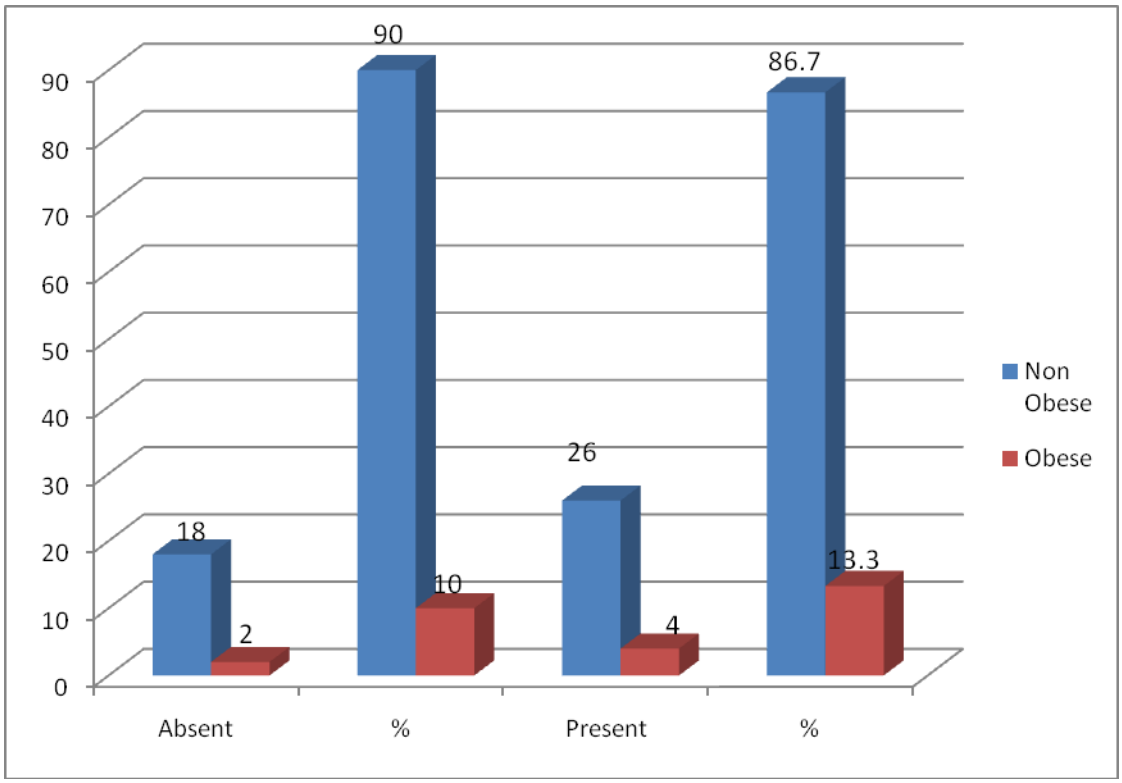


**Table No 7: Frequency & percentage distribution patients according to HTN**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **HTN** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 15 | 75.0 | 24 | 80.0 | 39 |
| Present | 05 | 25.0 | 06 | 20.0 | 11 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Graph NO 7: Frequency & percentage distribution patients according to HTN**

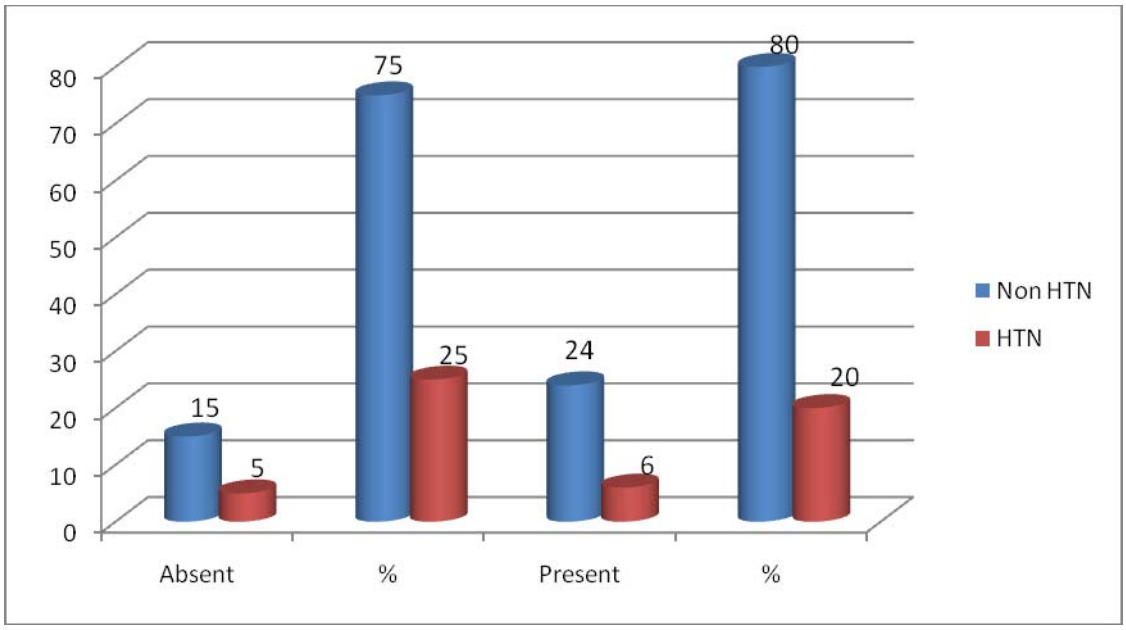


**Table No 8: Frequency & percentage distribution patients according to Anaemia**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **Anaemia** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 14 | 70.0 | 10 | 33.3 | 22 |
| Present | 06 | 30.0 | 20 | 66.7 | 28 |
| Total | **20** | **100** | **30** | **100** | **50** |

**TABLE NO 8: Frequency & percentage distribution patients according to Anaemia**

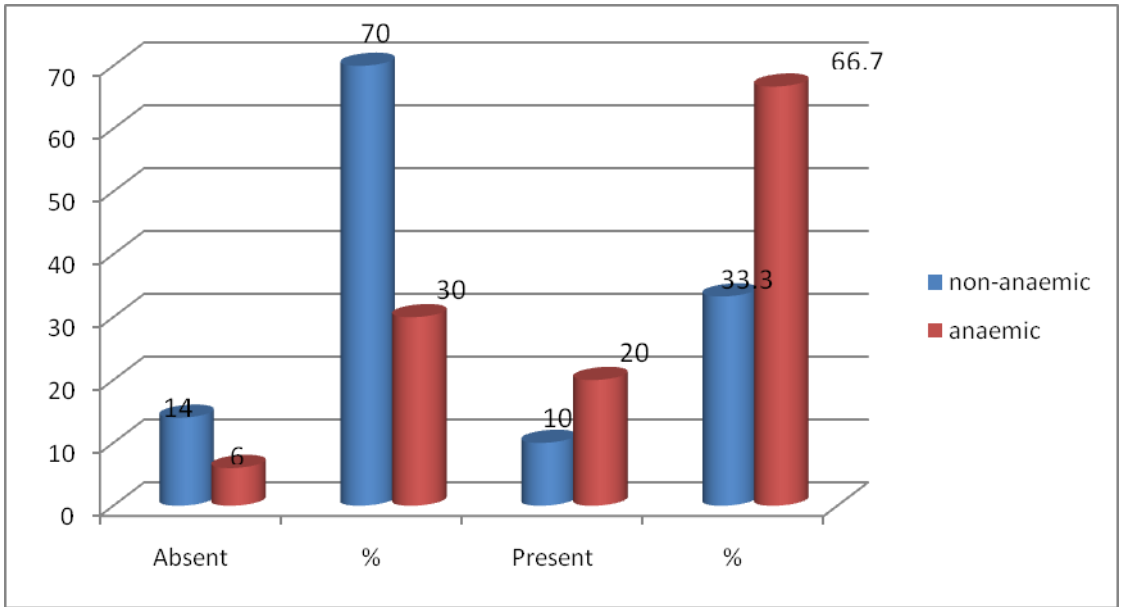


**Table No 9: Frequency and percentage distribution of patients according to DM**

| | HYPERHOMOCYTENEMIA | | | | |
|---|---|---|---|---|---|
| **DM** | **Absent** | **%** | **Present** | **%** | **Total** |
| Absent | 18 | 90.0 | 20 | 66.7 | 38 |
| Present | 02 | 10.0 | 10 | 33.3 | 12 |
| Total | **20** | **100** | **30** | **100** | **50** |

**Chart No 9 : Frequency and percentage distribution of patients according to DM**

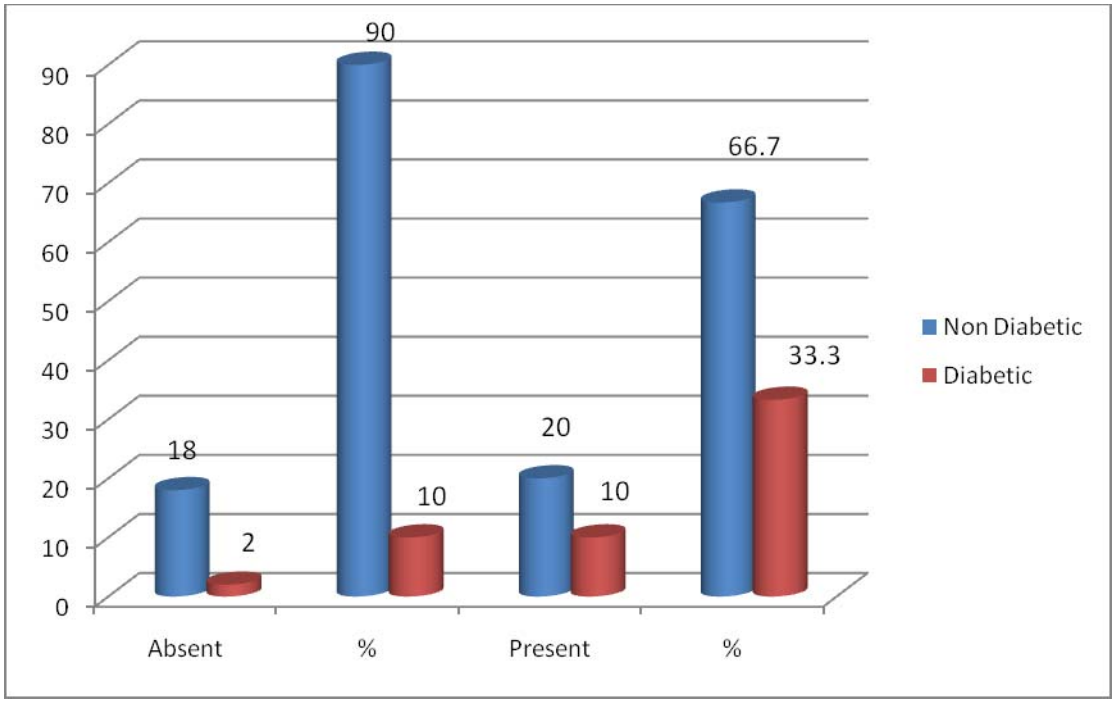


**Table No 10: Analysis of Data**

| S.I No. | HYPERHOMOCYTENEMIA | | D.F | Chi-square | p-value | Result |
|---|---|---|---|---|---|---|
| | Absent | Present | | | | |
| **Age (years )** | | | | | | |
| 24-43 | 08 | 15 | | | | |
| 44-63 | 07 | 07 | | | | |
| 64-83 | 05 | 08 | 2 | 0.857 | 0.651 | NS |
| **Gender** | | | | | | |
| Male | 11 | 14 | | | | |
| Female | 09 | 16 | 1 | 0.333 | 0.773 | NS |
| **Trauma** | | | | | | |
| Absent | 15 | 24 | | | | |
| Present | 05 | 06 | 1 | 0.175 | 0.676 | NS |
| **Immobilization** | | | | | | |
| present | 04 | 18 | | | | |
| absent | 16 | 12 | 1 | 7.792 | 0.005 | S |
| **Smoking /Tobacco Chewing** | | | | | | |
| Absent | 13 | 09 | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Present | 07 | 21 | 1 | 5.96 | 0.021 | S |
| **IHD** | | | | | | |
| Absent | 15 | 27 | 1 | 2.009 | 0.156 | NS |
| Present | 05 | 03 | | | | |
| **Obesity** | | | | | | |
| Absent | 18 | 26 | 1 | 0.126 | 0.722 | NS |
| Present | 02 | 04 | | | | |
| **HTN** | | | | | | |
| Absent | 15 | 24 | 1 | 0.175 | 0.676 | NS |
| Present | 05 | 06 | | | | |
| **Anaemia** | | | | | | |
| Absent | 14 | 10 | 1 | 6.46 | 0.02 | S |
| Present | 06 | 20 | | | | |
| **DM** | | | | | | |
| Absent | 18 | 20 | 1 | 3.58 | 0.058 | NS |
| Present | 02 | 10 | | | | |

NS = not significant S=significant

Table No 10 Reveals that there is no association between Hyperhomocystenemia with selected demographic variables such as age, gender trauma , IHD, HTN and DM as the p-value is more than 0.05. There is association between hyperhomocystenemia and risk factors like immobilization, smoking and anaemia, as p-value is less than 0.05.

# DISCUSSION

Hyperhomocystenemia is a proven risk factor for DVT. A case control study by Simioni et al showed that the prevalence of hyperhomocystenemia was 25%[36]. Another study by Den Heijer M showed the prevalence of hyperhomocystemia as 10%[18]. According to Wadia R et al, the prevalence of hyperhomocystenemia in Indians is between 52-84%[37]. In our study,the prevalence of hyperhomocystenemia in patients of DVT was 600 per thousand population. Thus our study shows that the prevalence of hyperhomocystenemia in patients with DVT is higher in Indian population as compared to the western population.

In a case control study, Falcon et al found that hyperhomocystenemia was a risk factor for thrombosis in patients younger than 40 years of age[6]. Hyperhomocystenemia is a risk factor for recurrent venous thrombosis in patients between 20 and 70 years of age, as compared with controls from the general population[7]. In our study, young patients with DVT had higher prevalence of hyperhomocystenemia as compared to older population but there was no statistical significance in the prevalence of hyperhomocystenemia among the different age groups.

Study by Y Unlu, S Keles and N Becit showed higher plasma levels of tHcy in men than women in all ages. The ratio of Hcy levels in male to female subjects was 1.2:1 [38]. Martin Den Heijer, Ted Koster, Henk J Blom et al showed that the odds ratio was twice as high for women as for men suggesting that women were more succeptible to the pathological effects of elevated homocysteine levels, although their homocysteine levels are in general lower than that of men[18]. However, in our study

the prevalence of hyperhomocystenemia was higher in the female population (53.3%) when compared to males(46.7%).

Claes Bergmark et al suggested that smokers have a higher level of homocysteine than non smokers. They also have lower levels of Vit B6[39]. Hyperhomocystenemia may increase smoking related platelet and clotting effects or exert a toxic effect on the endothelium. Furthermore, smoking lowered the levels of Vit B6 and folate which explains the increased levels of homocysteine in smokers[40]. This is consistent with our study, which shows a statistical significance between smoking and hyperhomocystenemia.

Hyperhomocystenemia is associated with three fold increased risk of IHD and coronary heart disease[41]. Study by Gautam V Kamat, S C Metgud, Vishwanath M Pattanashetti showed association between IHD and hyperhomocystenemia[42]. However, in our study no statistical significance was found between the same.

Some studies have demonstated an association between DM and HTN with hyperhomocystenemia. Study by Medha N Munshi, Angie stone, Louis Fink et al showed greater frequency of hyperhomocystenemia in patients with NIDDM(39%)as compared with age matched controls (7%)[43]. Also hyperhomocystenemia limits the bioavailability of nitric oxide, increases oxidative stress, stimulates the proliferation of vascular smooth muscle cells and alters the elastic properties of the vascular wall[44]. However in our study, no association was found between HTN, DM and obesity and hyperhomocystenemia.

In our study, a statistical association of hyperhomocystenemia with immobilization and anaemia was found.

# CONCLUSION

- The prevalence of hyperhomocystenemia in cases of deep vein thrombosis in our population was 600 per thousand cases.

- There was a statistically significant association between hyperhomocystenemia and immobilization, smoking and anemia .

- There was no association between hyperhomocystenemia and age, gender, IHD, HTN, DM and obesity in our study.

# SUMMARY

Hyperhomocystenemia is a known risk factor for the development of deep vein thrombosis. Various studies have been conducted in the western countries to know the prevalence of hyperhomocystenemia in patients with DVT in the general population. There are very few studies documenting the prevalence of hyperhomocystenemia in the Indian population. Thus this study was conducted to determine the prevalence of hyperhomocystenemia in cases of DVT in our population.

This was a cross sectional study with a total of 50 patients included in the study. DVT was confirmed by Doppler examination. Serum homocysteine was measured and the data was analyzed. Prevalence was calculated. Statistical significance was calculated using Chi Square test.

Of the 50 patients studied, 25 were males and 25 were females. The prevalence of hyperhomocystenemia among DVT cases was 600 per thousand population. There was no association between hyperhomocystenemia and risk factors like age, gender, IHD, HTN, DM and obesity in our study. A statistically significant association between hyperhomocystenemia and immobilization, smoking and anemia was found in our study.

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# ANNEXURES

## PROFORMA

| | |
|---|---|
| **Name:** | **CASE NO:** |
| **Age:** | **IP NO:** |
| **Sex:** | **DOA:** |
| **Religion:** | |
| **Occupation:** | **DOD:** |
| **Residence:** | |

**Chief complaints**

1) Pain: : Duration
2) Swelling of leg : Present/Absent Duration

**History of Presenting Illness**

1) Time of onset

2) Is it both legs?

3) Has there been any trauma?

4) Is there any pain? (65% below knee DVT are asyptomatic) - type of pain

5) Is there any swelling? How recent?

6) Have there been any skin changes?

7)Any odema anywhere else?

8) Is the patient mobile?

9) Recent surgery or trauma/fractures

10) Paralysis/paresis

11) Plaster immobilisation of lower limb

12) Recently bedridden for >3 days or major surgery <4 weeks

.

**Symptoms of PE**

Pleuritic, sharp chest pain

Acute onset of breathlessness

Haemoptysis

**Previous Medical History**

DVT or PE. Arthritis. Malignancy (ongoing treatment, within 6 months or palliative)

Thrombophilia. Recurrent miscarriages. Diabetes. MI. AF. CVA

**Family History**

DVT or PE. Cardiac problems. CVA. Clotting disorders

**Personal History**

smoker, pregnancy, long haul travel, obesity, immobility

**Drug history & Allergies**

Immunosuppressant drugs. HRT. Contraceptive pill. Warfarin. IV drug user

**Occupational history**

Travel or immobility

**General Physical Examination**

| | |
|---|---|
| Pallor | present/absent |
| Icterus | present/absent |
| Clubbing | present/absent |
| Generalized Lymphadenopathy | present/absent |
| Build | Poor/Middle /Well |
| Nourishment | Poor / Middle / Well |

**Vitals**

PR:

BP:

RR:

Temp:

**Local Examination**

Inspection – swelling of leg , level of the swelling.

Palpation – elicit tenderness (Homan's sign & Moses' sign)

**Limb girth measurements.**

**Systemic examination** –

CVS:-

RS :-

CNS:-

PA : -

**Investigations**

Blood: Hb% TC DC platelet count

Urine: Alb Sugar Microscopy

HIV: HBSAg: LFT RFT

Random blood sugar

Lipid profile

Colour Doppler

ECG

Chest X-ray

Plasma homocysteine levels

**Inference:**

# PARTICIPANT INFORMED CONSENT FORM

**TITLE OF THE PROJECT** - PREVALANCE OF HYPERHOMOCYSTENEMIA IN PATIENTS OF DEEP VEIN THROMBOSIS

**PRINCIPAL INVESTIGATOR** - DR. HARIKRISHNAN NAIR

**GUIDE** - DR. VIJAYA PATIL MS

**PURPOSE OF RESEARCH:**

I have been informed that this is a longitudinal study for detecting the prevalance of hyperhomocystenemia in cases of deep vein thrombosis. I have also been given a free choice of participation in this study. This study will help in proper understanding, regarding risk factors of deep vein thrombosis.

**PROCEDURE:**

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

**RISK AND DISCOMFORTS:**

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

**BENEFITS:**

I understand that my participation in this study will help analyse the prevalance of hyperhomocystenemia in deep vein thrombosis and help assess if homocysteine is a risk factor in deep vein thrombosis

**CONFIDENTIALITY:**

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

**REQUEST FOR MORE INFORMATION:**

I understand that I may ask more questions about the study at anytime Dr. Harikrishnan Nair is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

**REFUSAL FOR WITHDRAWAL OF PARTICIPATION:**

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. Harikrishnan Nair may terminate my participation in the study after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

**INJURY STATEMENT:**

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Dr.Harikrishnan Nair Date

(Investigator)

**STUDY SUBJECT CONSENT STATEMENT:**

I confirm that Dr. Harikrishnan Nair has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant / Guardian Date

_____ _____

Witness to signature Date

# ETHICAL CLEARANCE CERTIFICATE

Ethical Committee BIJAPUR-586103 27/2011 Date 21-10-11 Shri B. M. PATIL Medical College

*B.L.D.E. UNIVERSITY'S*

**SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103**

**INSTITUTIONAL ETHICAL COMMITTEE**

## *INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE*

*The Ethical Committee of this college met on* 20-10-2011 *at* 10-30am *to scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.*

*Title* "Prevalence of hyperhomocysteinemia in deep vein thrombosis"

—x—x—

*Name of P.G./U.G. student/Faculty member* Dr. Harikrishnan Nair. Dept of Surgery.

*Name of Guide/Co-investigator Dr.* Vijaya Patil, Assoc Prof Surgery.

DR.M.S.BIRADAR,
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Chairman
Ethical Committee
BLDEA'S Shri. B.M. Patil
Medical College
Bijapur-586103

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

# KEY TO MASTER CHART

| | | |
|---|---|---|
| **M** | **-** | **Male** |
| **F** | **-** | **Female** |
| **Nil** | **-** | **Absent** |
| **+** | **-** | **Present** |
| **IHD** | **-** | **Ischemic Heart Disease** |
| **HTN** | **-** | **Hypertension** |
| **DM** | **-** | **Diabetes Mellitus** |
| **HCY** | **_** | **Hyper Homocystenemia** |
| **Ext** | **-** | **External** |

M

| Sr. No | Name | Age | Gender | Trauma/Surgery | Immobilization | Smoking/tobacco | IHD | Obesity | HTN | DM | Anaemia |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Basanagowda Biradar | 50 | M | Nil | Nil | + | Nil | + | Nil | Nil | + |
| 2 | Ningappa | 83 | M | Nil | Nil | + | + | Nil | Nil | + | + |
| 3 | Basamma | 35 | F | Nil | + | + | Nil | Nil | Nil | Nil | + |
| 4 | Sidappa Kumbar | 80 | M | Nil | + | + | + | Nil | + | Nil | Nil |
| 5 | Bharat Angadi | 34 | M | Present | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 6 | Shranagowda Biradar | 30 | M | Present | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 7 | Shrikanth Hiremath | 65 | M | Nil | Nil | + | Nil | Nil | Nil | Nil | + |
| 8 | Janaki Boke | 24 | F | Nil | + | Nil | Nil | Nil | Nil | Nil | + |
| 9 | Mahadev Koppad | 75 | M | Present | + | + | Nil | Nil | + | + | + |
| 10 | suslabai | 80 | F | Nil | Nil | + | Nil | Nil | Nil | + | Nil |
| 11 | Danamma | 29 | F | + | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 12 | Geeta Biradar | 40 | F | Nil | + | Nil | Nil | Nil | Nil | Nil | + |
| 13 | Basalingawwa | 60 | F | Nil | Nil | + | Nil | Nil | + | + | + |
| 14 | shivagangawwa | 65 | F | Nil | + | + | Nil | + | + | + | + |
| 15 | Yallamma Hadapad | 25 | F | Nil | + | Nil | Nil | Nil | Nil | Nil | Nil |

| Sr. No | Name | Age | Gender | Trauma/Surgery | Immobilization | Smoking/tobacco | IHD | Obesity | HTN | DM | Anaemia |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | Paramanna Navi | 64 | M | Nil | Nil | + | Nil | Nil | + | + | Nil |
| 17 | Savita | 30 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | + |
| 18 | Yasheen Mulla | 42 | F | Nil | Nil | + | Nil | Nil | Nil | Nil | + |
| 19 | Shankremma | 30 | F | Present | + | Nil | Nil | Nil | Nil | Nil | Nil |
| 20 | Neelabai | 34 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 21 | Laxman | 45 | M | Nil | Nil | + | Nil | Nil | Nil | Nil | Nil |
| 22 | Ningappa | 65 | M | Nil | Nil | + | Nil | Nil | + | + | + |
| 23 | Laxman Koli | 46 | M | Nil | Nil | Nil | Nil | Nil | + | Nil | Nil |
| 24 | Mahadev | 69 | M | Nil | + | + | Nil | Nil | Nil | Nil | Nil |
| 25 | Nageshwar | 37 | M | Present | + | + | Nil | + | Nil | Nil | + |
| 26 | Ningaraj Hadapad | 60 | M | Nil | + | + | Nil | Nil | Nil | Nil | + |
| 27 | Yallawwa | 25 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 28 | Neelabai | 35 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | + |
| 29 | Neelawwa Akale | 75 | F | Nil | + | + | + | Nil | Nil | + | + |
| 30 | Shubhadra | 60 | F | Nil | Nil | Nil | + | + | Nil | Nil | Nil |
| 31 | Nagawwa Haivali | 60 | F | + | + | Nil | Nil | Nil | Nil | Nil | + |

| Sr. No | Name | Age | Gender | Trauma/Surgery | Immobilization | Smoking/tobacco | IHD | Obesity | HTN | DM | Anaemia |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 32 | Chinappa | 30 | M | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 33 | Kavita | 38 | F | + | + | Nil | Nil | Nil | Nil | + | + |
| 34 | Mallappa | 60 | M | + | + | + | + | Nil | + | Nil | Nil |
| 35 | Sidramappa | 50 | M | + | Nil | + | + | Nil | Nil | Nil | Nil |
| 36 | Basamma biradar | 35 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | + |
| 37 | Ninganagowda | 81 | M | Nil | + | + | + | Nil | + | Nil | + |
| 38 | Jayshree | 35 | F | Nil | + | Nil | Nil | Nil | Nil | Nil | Nil |
| 39 | Mallikarjun | 34 | M | Nil | Nil | + | Nil | + | + | + | + |
| 40 | Gouvanna Tonshyal | 48 | M | Nil | + | + | Nil | Nil | Nil | Nil | + |
| 41 | Nagaraj Hadanur | 46 | M | NIL | + | + | Nil | Nil | Nil | Nil | + |
| 42 | latadevi Biradar | 24 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 43 | mahdevi bykod | 63 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | Nil |
| 44 | laxmi chinava | 35 | F | Nil | Nil | Nil | Nil | Nil | Nil | Nil | + |
| 45 | parvatibai karade | 72 | F | Nil | nil | Nil | + | Nil | Nil | + | + |
| 46 | Sachin Babu | 45 | M | Nil | + | + | Nil | + | Nil | Nil | Nil |
| 47 | Rudramma | 58 | F | Nil | + | + | Nil | Nil | Nil | + | + |

| Sr. No | Name | Age | Gender | Trauma/Surgery | Immobilization | Smoking/tobacco | IHD | Obesity | HTN | DM | Anaemia |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 48 | Pramod Kulkarni | 28 | M | Nil | Nil | + | Nil | Nil | Nil | Nil | Nil |
| 49 | Ramesh Yallappa | 79 | M | Nil | + | + | Nil | Nil | + | Nil | Nil |
| 50 | subhash Bhimappa | 38 | M | Nil | Nil | + | Nil | Nil | Nil | Nil | Nil |

## ASTER CHART

| Doppler study | Homocysteine levels | Hcy |
|---|---|---|
| Thrombosis of  left deep femoral, common femoral, superficial femoral upto Ext illiac | 12.28 | Absent |
| Thrombosis of right deep femoral Vein | 27.3 | + |
| Thrombosis of left popliteal vein , deep femoral vein | 23.2 | + |
| Thrombosis of right popliteal and deep femoral vein | 13.71 | absent |
| Thrombosis of left popliteal vein , deep femoral vein, superficial femoral, common femoral vein upto External illiac with thrombosis of pelvic vessels | 4.32 | absent |
| Thrombosis of right popliteal and deep femoral vein | 11.95 | Absent |
| Thrombosis of right deep femoral Vein | 70 | + |
| Thrombosis of right popliteal and deep femoral vein | 13.38 | + |
| Thrombosis of left short and long saphenous vein, popliteal & deep femoral vein | 46.18 | + |
| Thrombosis of left popliteal, deep femoral and common femoral veins | 27.39 | + |
| Thromosis of popliteal and short saphenous veins | 16.31 | + |
| Thrombosis of left calf veins, popliteal and deep femoral veins | 26.64 | + |
| Thrombosis of right deep femoral Vein | 17.81 | + |
| Thrombosis of superficial femoral, deep femoral and common femoral vein extending upto proximal part of Ext illiac vein | 26.18 | + |
| Thrombosis of left Deep femoral vein | 27.45 | + |

| Doppler study | Homocysteine levels | Hcy |
|---|---|---|
| Thrombosis of deep and common femoral vein of right leg | 11.76 | Absent |
| Thrombosis of popliteal, deep, superficial femoral veins of right leg | 6.89 | Absent |
| Thrombosis of deep femoral veins of right leg | 41.26 | + |
| Thrombosis of calf veins and short saphenous vein of right leg | 12.01 | + |
| Thrombosis of deep femoral veins of right leg | 10.4 | Absent |
| Thrombosis of popliteal, superficial and deep femoral vein upto the ext illiac artery on left side | 12.43 | Absent |
| Thrombosis of deep femoral, superficial femoral and common femoral veins of the left leg | 28.1 | + |
| Thrombosis of deep femoral vein of left leg | 11.27 | Absent |
| Thrombosis of great saphenous and short saphenous veins and popliteal vein of right leg | 37.27 | + |
| Thrombosis of deep and common femoral vein of right leg extending upto Ext illiac vein | 59.99 | + |
| Thrombosis of common femoral vein of left leg | 43.52 | + |
| Thrombosis of popliteal and common femoral veins of left leg and of popliteal vein, deep femoral and superficial veins of right leg | 9.3 | Absent |
| Thrombosis of the popliteal and short saphenous veins of Right leg | 5.65 | Absent |
| Thrombosis of the popliteal and deep femoral veins of left leg | 21.25 | + |
| Thrombosis of popliteal and deep femoral veins of left leg | 8.94 | Absent |
| Thrombosis of deep and common femoral vein of left leg | 11.76 | Absent |

| Doppler study | Homocysteine levels | Hcy |
|---|---|---|
| Thrombosis of right peroneal, popliteal, deep and common femoral vein of left leg including the Ext illiac vessel | 11.5 | absent |
| Thrombosis of Popliteal and superficial femoral vein of left leg with thrombosis of great and short saphenous veins of left leg | 25.3 | + |
| Thrombosis of the deep and common femoral vein of left leg | 18.68 | + |
| Thrombosis of popliteal and deep femoral veins of right leg | 3.91 | Absent |
| Thrombosis of common femoral vein of left leg | 20.3 | + |
| Thrombosi of deep femoral, superficial and common femoral vein of right leg extending upto Ext illiac vein | 19.99 | Absent |
| Thrombosis of right deep femoral Vein | 16.24 | + |
| Thrombosis of left deep and common femoral vein | 25.8 | + |
| Thrombosis of popliteal and deep femoral vein of left leg | 54.02 | + |
| Thrombosis of left deep and common femoral vein | 52.02 | + |
| Thrombosis of popliteal, deep, superficial femoral veins of right leg | 6.84 | Absent |
| Thrombosis of popliteal and common femoral veins of left leg and of popliteal vein, deep femoral and superficial veins of right leg | 8.9 | Absent |
| Thrombosis of right deep femoral Vein | 12.5 | + |
| Thrombosis of the popliteal and deep femoral veins of left leg | 15.18 | absent |
| Thrombosis of left deep femoral, common femoral, superficial femoral upto Ext illiac | 17 | + |
| Thrombosis of right deep femoral Vein | 18.21 | + |

| Doppler study | Homocysteine levels | Hcy |
|---|---|---|
| Thrombosis of popliteal, deep and common femoral vein of right leg including the Ext illiac vessel | 110 | + |
| Thrombosis of deep femoral, superficial and common femoral vein of right leg extending upto Ext illiac vein | 11.14 | absent |
| Thrombosis of deep femoral veins of right leg | 42.15 | + |