"AN OBSERVATIONAL STUDY TO DETERMINE THE INCIDENCE OF LOWER LIMB DEEP VEIN THROMBOSIS AFTER MAJOR ORTHOPAEDIC SURGERIES"

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ACCEPTANCE LETTER

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LIST OF ABBREVIATIONS USED

DVT	–	Deep vein thrombosis
BMI	–	Body Mass index
VTE	–	Venous thromboembolism
PT	–	Prothrombin time
PE	–	Pulmonary embolism
VKA	–	Vitamin K Antagonist
HMWH	–	high molecular weight Heparin
STP	–	Superficial thrombophlebitis
IL-6	–	interleukin 6
CRP	–	C Reactive protein
HF	–	Heart failure
THR	–	Total Hip Replacement
TKR	–	Total Knee Replacement
IVC	–	Inferior vena cava
OCPs	–	Oral contraceptive pills
DM	–	Diabetes mellitus
CKD	–	chronic kidney disease
CLD	–	Chronic liver disease
ATV	–	Anterior tibial vein
PTV	–	Posterior tibial vein
PTS	–	Post thrombotic syndrome

ABSTRACT

"An observational study to determine the incidence of Deep vein thrombosis after major orthopaedic surgeries"

Introduction

Deep Vein Thrombosis (DVT) is one of the common medical conditions in case of traumas. It should be diagnosed and treated as early as possible to prevent complications like chronic pain, varicose veins, ulcers, by which the quality of life can be affected. Deep vein thrombosis can also lead to fatal pulmonary embolism. Clinical signs can be insensitive to diagnose Venous thromboembolism (VTE) especially true in case of lower limb trauma as leg swelling, pain, chest pain and breathlessness all can occur due to injury per se. The reason for low reporting of incidence of DVT among Indians is due to unawareness among patients and lack of availability of diagnostic facilities. So many cases remain undiagnosed.

There is sufficient data regarding incidence of deep vein thrombosis in western world. In India much studies have not been conducted on this subject so exact incidence of DVT after major orthopaedic surgeries is not known.

Aims and objectives

Primary objectives

1) To determine incidence of lower limb DVT after major orthopaedic lower limb surgeries.

Secondary objectives

1) To identify risk factors for deep vein thrombosis, such as diabetes, hypertension, smoking, and obesity.

Material and methods

The present study was conducted in KLES Dr Prabhakar Kore hospital and medical Research centre, Belagavi after obtaining the ethical committee approval

Study Design

Hospital based 1 year observational study

Study period – 1st January-31st December 2020

Source of data

Patients undergoing major orthopaedic surgeries admitted in the department of orthopaedics at the KLES DR. Prabhakar Kore Hospital and Medical Research Centre and Charitable Hospital, Belagavi in between 1st January 2020 to 31st December 2020, over a period of one year. 42 subjects were included into the study after inclusion and exclusion criteria. Pre operative and post operative color doppler was done (POD-5) as a diagnostic modality to determine incidence of DVT.

Data analysis

Data is analysed using statistical software **R version 4.0.2** and **Microsoft Excel**. Continuous variables were represented by mean± sd/median (range) and categorical variables represented by frequency and percentage. To check the association between categorical variables Chi-square test is used. To compare mean/distributions between groups t-test/Mann-Whitney test is used. P-value less than or equal to 0.05 indicates statistical significance.

Results

In the study there were 42 subjects, with age 51.12±20.09 years. There were 15 females and 27 males in the study. Among 42 subjects 18 subjects were diagnosed with hip fractures, 10 subjects were diagnosed with tibia shaft fractures, 2 were diagnosed with ankle fractures, 7 were diagnosed with femur shaft fractures, 4 were

diagnosed with fractures around knee joint and 1 was diagnosed with pelvis fracture. Post operatively 9 subjects had DVT. Among 9 subjects 6 had fractures around hip joint, 1 had femur shaft fracture, 1 fracture around knee joint and 1 had pelvic fracture. Incidence of DVT after major orthopaedic surgeries was observed as 21.4%. Smoking, alcohol intake, diabetes mellitus, BMI >25 were the risk factors for development of DVT. Out of 9 DVT patients 7(77.78%) were smokers p value of 0.0004998, 6 had history of alcohol intake, p value of 0.0009995, 7(77.78%) p value of 0.0004998 were diabetics, 8 (88.89%) p value of 0.001499 had BMI >25.

Conclusions

This study shows that there is high incidence of DVT in elderly age group with co morbid conditions like diabetes mellitus and among smokers and alcoholics. Among fracture types hip fractures were more commonly associated with DVT. So routine color doppler should be done as a screening tool among elderly age group with comorbid conditions after surgeries around hip joint. By screening patients for DVT deadly complications like pulmonary embolism and other complications can be prevented by timely and appropriate treatment.

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INTRODUCTION

Deep vein thrombosis (DVT) is common medical condition which is associated with considerable morbidity and mortality. Major medical problems associated with DVT include death, post-thrombotic syndrome, right ventricular dysfunction, increased right arterial pressures and the risk of recurrent DVT. [1,2] The risk factors for DVT include pregnancy, hormone replacement therapy, prolonged immobility, obesity, increasing age and long bone trauma[3,4]. There are many sporadic reports concerning the incidence of DVT but a systematic basis for diagnosing and preventing its complications has not been established. The venogram and ultrasound has been verified as the modalities for detecting DVT. [5]

Deep Vein Thrombosis (DVT) is defined as formation of thrombus in one of the veins in body.[6]

DVT can lead to various complications which may be life threatening like Pulmonary Embolism (PE), Post thrombotic syndrome (PTS), chronic venous ulceration.[7]

There is enough data available in western world regarding incidence of DVT. In India, we don't have enough data about the incidence of DVT due to various reasons like lack of availability of diagnostic modalities and unawareness among doctors.[8]

The clinical signs and symptoms are not specific to diagnose DVT as pain and tenderness in the calf muscles can be due to injury per se so we need to study about incidence about DVT after major orthopaedic surgeries in Indian scenario to establish guidelines which can reduce mortality and morbidity among patients by the diagnostic modality which is readily available, has high sensitivity and specificity and doesn't have major limitations.[9] Contrast Venography is the gold standard to diagnose DVT

but it has various complications like contrast related anaphylactic reactions, acute renal failure.[10]. Its major disadvantage is that it is invasive method. In this study, we have done pre and post-operative color doppler which has high sensitivity and specificity and it is a non-invasive method.[11] By conducting this study, we want to establish that if color venous doppler be made as screening tool after every major lower limb orthopaedic surgery.

AIM AND OBJECTIVES

Primary objectives

1) To determine incidence of lower limb DVT after major orthopaedic surgeries.

Secondary objectives

1) To identify risk associations for DVT, such as diabetes, hypertension, smoking and obesity.

REVIEW OF LITERATURE

DVT is medical disorder characterized by formation of the thrombi in venous system which may lead to PE. Generally, it is believed that thrombus formation occurs at legs but it may occur at arms [11]

PATHOGENESIS OF THROMBUS

Virchow first described the pathological basis regarding formation of thrombus in 1856.

"Virchow's triad" [12]

1) Venous stasis

2) Vascular injury

3) Hypercoagulability

Venous thrombosis occurs at sites adjoining valves, where there is sluggish flow, consequently there is elevation of haematocrit value. Hypercoagulable microenvironment is created resulting in down regulation of antithrombotic proteins which prevent thrombus formation normally. On valves there is expression of antithrombin factors. Anti-thrombin factors include thrombomodulin molecules. Due to venous congestion, there is hypoxia which increases certain procoagulant factors like P-selectin. P-selectin acts as adhesion molecule, it interacts with the immunologic cells containing tissue factor. Endothelial cells or cells outside the extravascular system express tissue factor. Tissue factor act as focal point for thrombosis.

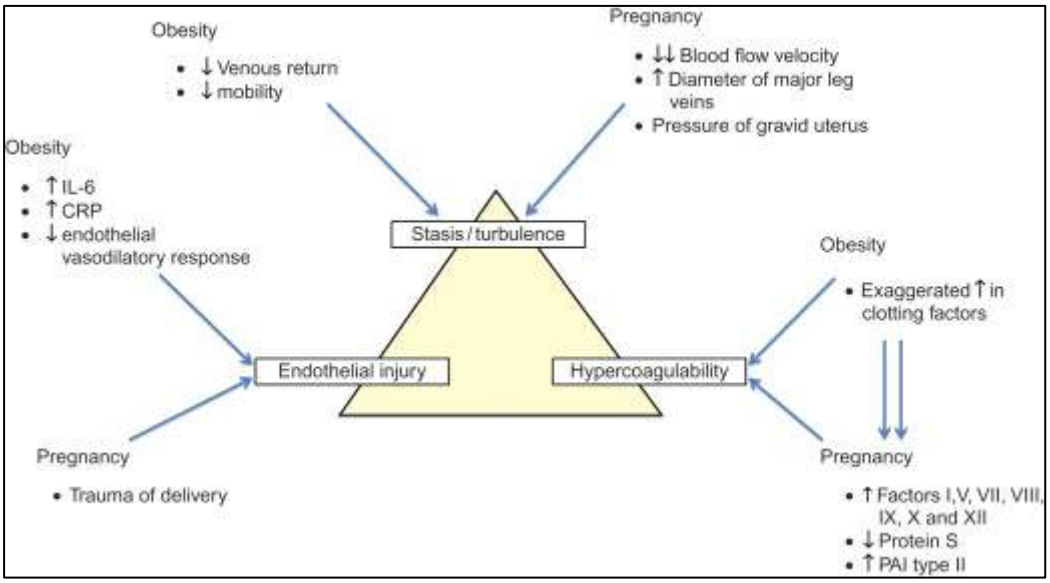


Figure 1: Pathogenesis of Thrombosis

Structure of thrombus [12,13]:

Area of thrombus include

Red area

White area.

Red region is the site of cellular attachment. It is area for thrombus expansion. RBCs along with fibrin molecules constitutes red part.

Platelet along with fibrin units constitute the white area. White patches are thrombus propagative zones, which cause the thrombus size to grow. Platelet-induced clot shrinkage factors compresses RBCs into various shapes like polyhedrocytes, intermediate shaped RBCs. RBCs which are not compressed lead to biconcave cell formation. There is extremely small gap between these fibrin structures.

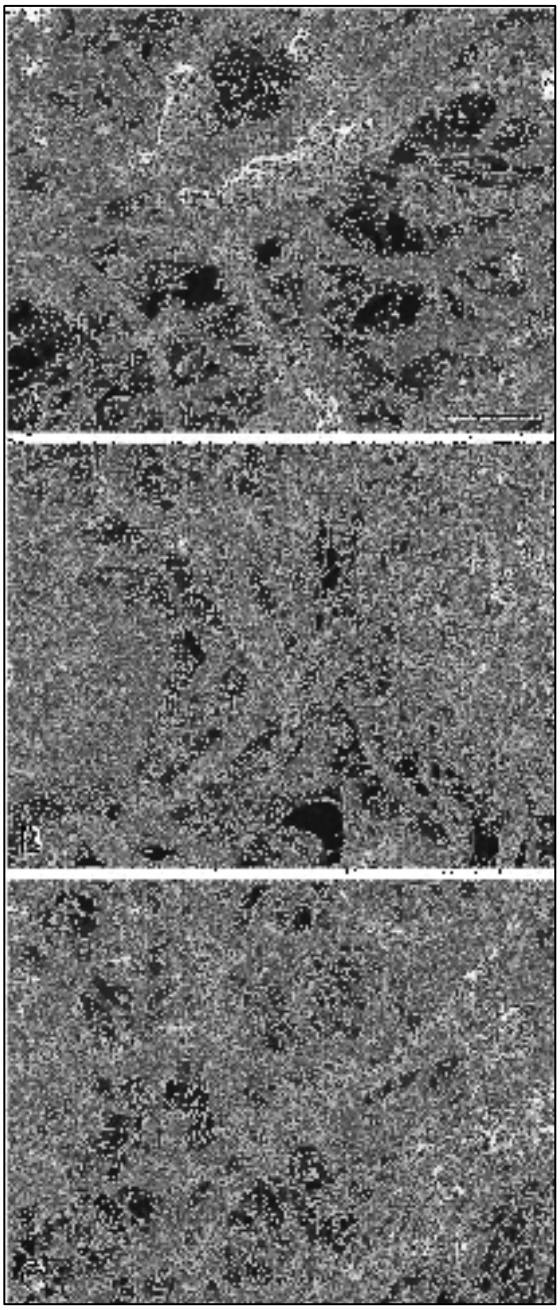


Figure 2: Structure of thrombus

Venous system[14]:

Venous system is categorized into 3 main groups. Muscular fascia surrounding the calf and thigh muscles helps in categorization of veins.

1) Deep veins
2) Superficial veins
3) Perforating veins

Veins above fascia are known as superficial veins. Veins below muscular fascia are known as deep veins, veins that pierces muscular fascia are known as perforating veins.

Histologically, veins constitute 3 layers

1) Tunica intima
2) Tunica adventitia
3) Tunica media.

Veins have much weaker muscular layer then arteries. There is proper demarcation of these layers in veins but not so in arteries. Veins correspond to respective arteries and sub-categorized as small, large and medium.

Cutaneous microcirculation is done by superficial veins. Deeper structures are drained by deep veins. Perforating veins establish connection between them.

Valves are special regulators which prevent backflowing of blood. Veins contain these regulators whereas arteries don't. When these regulators don't function properly, it leads to condition known as varicose veins.

Deep veins-

1) Anterior tibial vein (ATV)
2) Posterior tibial vein (PTV)
3) Peroneal vein

Drainage of anterior compartment of leg is done by ATV. ATV is the forward continuation of dorsal pedal vein. This vein can be located between tibia & fibula above interosseous membrane. Drainage of posterior compartment of leg is done by PTV. This vein is more superficial at posterior region of medial malleolus hence it is located there.

ATV and PTV join together to form popliteal vein (PV) at lower border of knee. Popliteal artery (PA) is lateral to popliteal vein (PV) at knee joint. Femoral vein is extension of PV at adductor hiatus.

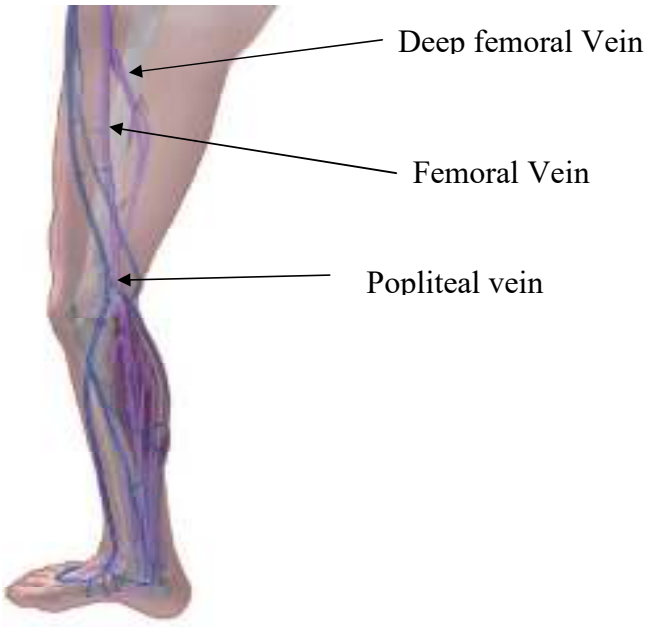


Figure 3: Anatomy of deep veins

Perforating veins [15]:

Perforating veins establish connection between deep & superficial venous systems. Nomenclature of perforating vein is based on the location where they are located, in the ankle they are termed as ankle perforators, while in leg, they are called as leg perforators, in knee, they are known as knee perforators and in thigh, they are termed as thigh perforators. Further sub grouping of perforators is on the side where they are present like anterior perforator, posterior perforator, medial perforator and lateral perforator. Whenever there is insufficiency in these veins it will leads to medical condition known as varicosities.

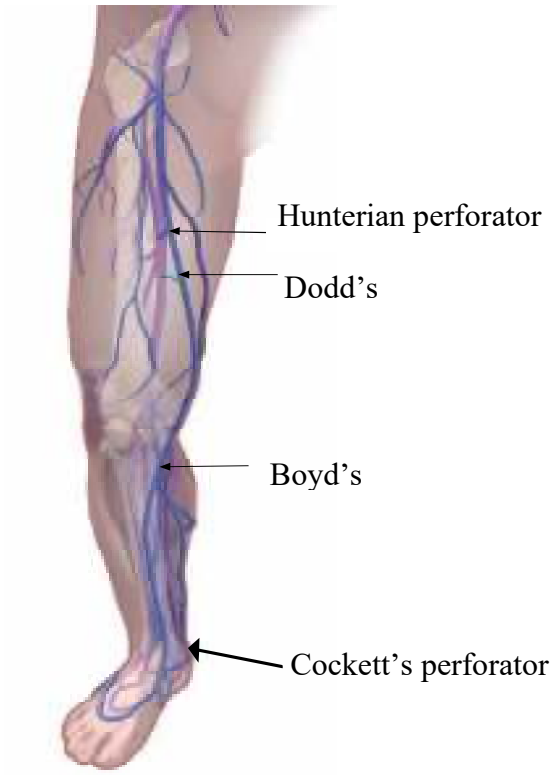


Figure 4: Perforators of lower limb

DVT INCIDENCE:

Junyong Li et al.[16] conducted prospective study for determining incidence of DVT in tibia plateau fractures patients. Duplex sonography was performed for diagnosing thrombosis. From the database of orthopaedics department data was gathered. 47 patients out of 987 patients were confirmed with DVT with incidence of 4.7% after doppler evaluation. Limitations in this study were firstly, factors like time duration of immobilisation of fractures extremity before and after operative procedure, were not involved so association of these factors with DVT could not be established. Secondly, link between some uncommon medical diseases and comorbidities involved with DVT couldn't be established. Thirdly, heparin was taken by patient pre-operatively which underestimated incidence of DVT.

Zhanchao Tan et al.[17] conducted study to evaluate DVT incidence following management of patella fractures. 716 subjects took part in study. For data collection of subjects, clinical & demographic medical records were analysed. For diagnosing DVT, doppler USG was performed. DVT was present in 29 out of 716 subjects, indicating a 4.1 percent DVT incidence rate. Prolonged surgical time, arrhythmias, loss of blood were determined as risk factors which contributed to DVT. It was inferred from this study that DVT incidence is high following patella fracture management so prophylaxis is advised routinely. The study's limitations were as following: firstly, their study was retrospective, which impacted the data's precision. Secondly, certain instances were abandoned at random due to missing data, which have affected the results. Finally, Doppler UGS screening was performed exclusively on patients who had clinical signs of DVT.

Luo Zixuan at al. [18] conducted study to evaluate DVT incidence in lower limbs after fractures around ankle joint. Study was retrospective in nature. 1451 individuals

with diagnoses of fractures around ankle were included in study. All subjects underwent operative procedures. Data gathering was done with medical record system. Type of data which was collected was demographic and surgery related. Multivariate logistic analytic approach recognized risk factors. DVT was diagnosed in 38 out of the 1451 individuals, representing incidence of DVT after ankle surgeries to be 2.6 percent. In eight cases, DVT affected both the operated and non-operated limbs (21.1%). Several limitations of study were, firstly, the retrospective methodology of study compromised the accuracy of data gathering, particularly for comorbid conditions that patients self-reported. Patients having insufficient or absence of records were removed from study. Secondly, certain factors like time duration of immobilisation of traumatic limb, the prophylactic administration of antithrombotic drugs, application of tourniquet during the operating procedure were not considered.

Khua zao et al.[19] conducted a study for determining incidence of DVT and risk factors for postoperative DVT development following operative procedures for IT fractures. Database of hospital on hip fractures was used to gather data. 1672 subjects who had operative management for IT fracture at hospital between month of Jan 2016 and month of December 2019 were recruited. Preoperative laboratory values, demographic data & data related to surgery were analysed. Following intertrochanteric surgery, incidence of DVT was 11.5 percent. This study's multivariate analysis determined that increasing age, operation duration (> 197 minutes), anaesthetic type and comorbidities (three) were all risk aspects for DVT. DVT incidence was high after intertrochanteric surgeries. This study was single-hospital based study with some inherent flaws like comorbidities and coagulation system deficiencies, were not looked upon in this study.

Seung Yeol Lee et al.[20] conducted a study to establish incidence of DVT and risk factors for DVT after major orthopaedic surgeries and concluded the total yearly incidence of DVT to be seventy per 1 lakh persons/year. It was inferred that risk of DVT increases with age. Patients aged between fifty to sixty-nine years had a fivefold higher risk for DVT than patients aged 49 years, and patients aged >70 years had a tenfold higher risk. In their study DVT was present more in women as related to men. There were few restrictions of study that should be noted- First, the information was gathered based on diagnostic codes not by individual patients, so research didn't govern if DVT episodes were repeated in same person. Furthermore, cases of bilateral surgery were not investigated. Second, the study's outcomes were predisposed by the DVT prophylaxis regimen and prevention programmes, and given the study's nature, consistency of the prophylaxis protocol was not established. The prevailing outcomes do not reflect the actual postoperative DVT incidence without prophylaxis. Third, DVT can be diagnosed with ultrasound, venography, or CT angiography in today's practise. The diagnostic technique could have exaggerated DVT incidence because venography has a much higher sensitivity than ultrasonography.

Bin-Fei Zhang et al.[21] conducted a study to evaluate DVT incidence before & after managing hip fractures in individual with lower extremities. Doppler USG was performed for diagnosing DVT. Two groups, thrombotic group and non-thrombotic group were established based on Doppler findings. The study involved 463 subjects with hip fractures. All were administered with LMWH at admission. The average age in their study was around 72.86 years. There were 288 females and 175 males among the 463 subjects. Intertrochanteric fractures were diagnosed in 218 subjects, subtrochanteric in 17 subjects, and neck femur in 228 subjects. In 278 subjects open reduction was performed. Hemiarthroplasty was done for 156 subjects, THR for 28

subjects, and external fixation for 1 subject respectively. DVT was present in 162 of the 463 individuals. There were 82 intertrochanteric fractures, 7 subtrochanteric fractures, and 73 neck femur fractures among 162 DVT patients. The incidence DVT on opposite side turned to be 13.60 percent.

Kapoor CS et al.[22] conducted a study in Indian population for determining DVT prevalence and its associated complications. In total of 125 patients, 106 were males & 19 were females. Out of total subjects, six patients were diagnosed with thrombosis of deep veins (4.8%). Out of DVT patients two patients had proximal thrombosis & two had distal thrombosis. 1 Patient had pulmonary embolism. They concluded that prevalence in Indian people is low so routine prophylaxis is not obligatory.

Sharma Harsh et al.[23] conducted study among Indian population. 112 subjects with lower limb fractures were included in the study. Patients underwent operation according to fractures patterns. The colour Doppler USG was performed as diagnostic modality pre-operatively and post operatively to detect thrombosis in veins. No pre operative prophylaxis was given. They noted significant DVT incidence of 19.6% after lower limb fracture surgeries.

Takkahiro Niikura et al.[24] undertook retrospective study in Japanese population for determination of incidence of DVT after pelvic fractures. 46 subjects with pelvic fracture were analysed for DVT. CT venography was performed as diagnostic modality for diagnosing DVT. High incidence (41.3 percent) of DVT was observed after pelvic surgeries in their study.

Chan K Y et al.[25] conducted a study in Chinese population for determining incidence of DVT after hip surgeries. Serial duplex USG was performed for

establishing diagnosis of DVT. 100 patients with hip fractures participated in the study. Among 100 subjects, 5 developed DVT after hip surgeries. Incidence of DVT in their study was 5% after hip fracture surgeries.

Saket R et al[26] did a study in Indian populatin to determine incidence of DVT after proximal fractures of femur. 66 subjects were enrolled in the study. DVT was present in 9 subjects among 66 subjects.

My Hanh Bui et al.[27] conducted a study to determine incidence of DVT in Vietnamese population. They involved 92 subjects with fractures of lower limb in their study. They performed colour Doppler pre & post operatively on fractured limb. Incidence of DVT in their study was 7%. Various risk aspects for DVT involved in the study were old age, extended duration of immobilization.

Ya-Hui Fu et al.[28] conducted retrospective observational study to calculate underestimated DVT incidence after neck femur surgery. They believed that true DVT incidence is underestimated after neck femur surgeries. They performed Doppler USG before & after surgery. Patients were grouped either in thrombotic group or in non-thrombotic group. They noted incidence of DVT to be 32 percent before surgical procedure & 56 percent after surgical procedure.

Thanainit C et al.[29] conducted study to determine incidence of DVT after hip surgeries. In total ninety-six patients with age of more than 60 years with fractures of hip participated in study. Bilateral contrast venography was performed for diagnosing DVT. Before performing contrast venography creatinine levels were checked. 47.9 percent of patients developed DVT after hip surgeries.

Ren Zhixin et al.[30] conducted retrospective case control study for determining incidence of DVT after femur shaft fracture surgeries. 308 patients with femur shaft fractures were included in study. DVT incidence after femur shaft fracture surgeries

was 15.6 percent. Higher D-dimer, blood loss, smoking and intra-operative loss of blood were determined as risk factors.

Dhillon K.S et al.[31] conducted prospective study in Malaysian population to evaluate incidence of DVT after fractures around hip. 88 patients participated in study. Bilateral venous contrast venography was performed for diagnosing DVT. Incidence of DVT determined after fractures around hip was 62.5%. They recommended regular prophylactic agents subsequent to hip surgeries.

Lim Y et al.[32] conducted study to evaluate Incidence of DVT after hip fracture surgeries. Doppler USG was performed on 5th post operative day. Total of 95 patients who underwent surgeries for hip fractures were included in their study. The incidence of DVT after hip fractures was 8 percent. Smoking, BMI >25, alcohol intake and higher BMI were associated risk factors for DVT.

Piovella F et. al.[33] conducted a study for determination of DVT in Asian population by performing contrast venography. Total of 96 patients underwent surgeries for hip fractures. Incidence of DVT after hip fractures was determined to be 42%.

Park J S et al.[34] conducted a study for determining DVT subsequent to fractures of hip joints. Total of 901 patients were enrolled for study, 337 received thrombophylactic agents by guidelines established by their institute. Remaining did not obtain any prophylactic treatment. 2.7 % of patients developed thrombosis and 1.4% developed PE. They concluded thrombophylactic drugs reduce incidence of DVT.

Mavalankar AP et al.[35] conducted a study in Indian population to determine incidence of DVT after hip surgeries. Study included 125 Indian patients who underwent fracture hip surgeries. Color doppler USG was performed to diagnose

DVT. Out of 125 study subjects 9 (7.6%) developed thrombosis in deep veins after hip surgeries.

Abelseth, G et al.[36] did prospective research to evaluate DVT incidence in patient undergoing surgeries distal to hip joint. 102 study participants were recruited for this research. All study subjects underwent surgeries for respective fractures. For all study participants, bilateral venography was performed for diagnosing DVT. They determined the incidence of DVT of 28 % after orthopaedic surgeries. It was highest after tibia plateau fractures followed by femoral shaft fractures and was least in tibia plafond fracture.

Singh R et al.[37] did a study to determine incidence of DVT after knee and hip surgeries. Doppler USG was performed to determine incidence of DVT. For the study, 182 subjects were involved. Incidence of DVT determined in this study was 18.2% of after hip and knee surgeries.

Ali Z et al.[38] conducted a study by involving 191 Indian patients with hip & knee fracture. Doppler USG was performed pre operatively and post operatively for diagnosing DVT. Occurrence of DVT was seen in 27% of patients.

RISK FACTORS:

Modifiable risk factors include:

1) Obesity
2) Elevated homocysteine levels
3) Surgeries
4) Type of anaesthesia used
5) Trauma
6) Pregnancy
7) Travel history
8) Oral contraceptive pills

Genetic factors for DVT include:

1) Connective tissue disorders
2) Factor v deficiency
3) Antithrombin deficiency
4) Elevated D-dimer
5) Prothrombin 20210A mutations
6) Elevated factor VII
7) Elevated factor IX
8) Elevated factor XI

1) Obesity [39]

The most essential biomarker tool used for obesity is BMI. The standard BMI ranges between 18 and 24.9 kilos per square metre. With obesity, risk of DVT increases by 2-3 times. BMI value of 25-29.9 is considered overweight. DVT risk increases when obese individuals are on oral steroids, OCPs. Body parameters like waist circumference play crucial role in DVT. It impairs venous return resulting in venous stasis. Each 1kg/m^2 rise in BMI increases risk for DVT significantly. When BMI exceeds 35kg/m^2, DVT risk increases by 8 times. Obesity can lead to recurrent DVT. Eichinger et al. conducted study to investigate relation between DVT & obesity it was found that frequency of DVT is about 9.3% among normal BMI patients and 17.5% in obese patients. There is excessive metabolism of adipocytes resulting in release and delivery inflammatory adipocytokines. Many reactive molecules are formed when FFAs are metabolised in liver. Endothelium is damaged and activated by reactive agents, which may lead to systemic coagulation.

2) Homocysteine levels [40]

Elevated homocysteine levels increase the risk for DVT. Homocysteine levels are elevated because of deficiency in vitamin B12, vitamin B6 and folate deficiency.

Homocysteine levels can also be elevated as an outcome of genetic deficiency of cystathione beta synthase.

Homocysteine levels that are very high can damage blood vessels, causing endothelial injury. Vitamin like B12, B6, and Folinic acid can reduce homocysteine levels. Screening for DVT in homocysteine elevated patients should be done. According to study conducted by Hainaut et al., homocysteine levels were high in 11.2 percent of VTE.

3) Surgeries [41]

The category and time duration of surgeries play important role in DVT development. Risk increases when duration of surgery increases by 60 minutes. Usage of tourniquet can produce direct compression of veins, resulting in venous sluggishness thus promoting coagulation. Factors like tissue thromboplastin released from injured soft tissues, dissection, reaming of bones orthopaedic procedures also promote coagulation. Surgical procedures cause prolonged immobility, resulting venous stasis which is the risk factor for DVT.

4) Type of anaesthesia [42]

DVT occurrence is also predisposed by anaesthetic type utilised. Epidural anaesthesia considerably reduces post-operative discomfort, allowing for early mobilisation and dropping the chances of DVT development.

5) Malignancy [43]

Malignancy is hypercoagulable state. Tumour cells have ability to stimulate coagulation cascade. Cells can produce the inflammatory factors and procoagulant factors which promotes coagulation. Tumour cells physically interact with blood cells (platelets, monocytes) & vascular cells to promote thrombus formation. Generation of acute phase reactants and aberrant protein metabolism are further pathways for DVT

formation in malignancies. Tumours can physically compress blood vessels leading to stasis of blood which promotes thrombus formation. Hormonal anticancer therapy can intensely increase thromboembolic events through different mechanisms, which include release of procoagulant factors, endothelium damage, or host cell stimulation of TF production.

6) Trauma [44]

Traumatic injury leads to various physiological changes that puts patient at elevated risk for DVT/VTE. Traumatic injury results in production cytokines like IL-6 which are inflammatory and prothrombotic, which promotes thrombus formation. Trauma causes immobilization leadings to stasis in veins thus promoting thrombus formation.

7) Pregnancy [45]

Relation between DVT and pregnancy is well documented due to hypercoagulable state of pregnancy. It is estimated that pregnant women are more likely to have DVT. Hypercoagulable environment supports body to prevent miscarriage by preventing excessive bleeding. DVT association is same in 1st trimester, in second trimester & in third trimester. Occurrence also increases throughout the first to six weeks of post- partum delivery. DVT risk further increases with obesity, older age, nulliparity, multiple gestations and immobility. Prothrombotic factors increase in pregnancy leading to prothrombotic state.

All the three constituents of Virchow's triad are seen in pregnancy.

1) Venous stasis is promoted due to two factors namely hormonal factor which reduces the venous muscular tone and mechanical which involves compression of vessels by enlarged uterus.

2) Endothelial damage occurs in veins of pelvis due to venous hypertension

3) Hypercoagulable condition is established in prenatal period. Fibrin release is augmented and fibrinolytic activity is diminished. Production of clotting factors is exaggerated in pregnancy.

8) Connective tissue disorders (CTDs) [46]

CTD like SLE, Rheumatoid arthritis, Antiphospholipid disorder, IBD, Celiac disease, and Wegner's granulomatosis are related with increased risk for DVT/VTE. Inflammation is common feature in all CTDs. Inflammation and coagulation pathways are interrelated to each other. Hypercoagulability results from inflammatory response by activation of prothrombotic factors, IL-6 production, endothelial dysfunction, inhibition of protein 6 system. Evidence of SLE and increased risk of DVT is documented. It is established that antiphospholipid antibodies are seen in SLE patients.

9) Inherited thrombophilia [47]

In a healthy body, balance between procoagulant & anticoagulant factors is well maintained. Nevertheless, in some hereditary conditions, there is imbalance between these components, increasing the risk for thrombosis. Several types of thrombophilia are -

1) Factor V mutation
2) Deficient Protein S
3) Prothrombin gene mutations
4) Deficient protein C

They all are polygenic and autosomal recessive having variable penetrance. In two to ten percent of normal population these mutations are present but these mutations are rare among African and Asian populations. In 1-4 percent of population, prothrombin G20210A is detected. Population with G20210A has a greater prothrombin concentration.

10) Heart failure (HF) [48]

Heart failure is a condition where metabolic demands of body are not fulfilled. Procoagulant state is seen in HF. There are many mechanisms for procoagulant state in HF. These include venous stasis due to reduced myocardial contractility, decreased mobility of patient, increased intracardiac pressure. Alikhan et al. reported DVT prevalence of 14 percent in HF patients which were hospitalized.

11) Diabetes mellitus [49]

Hyperglycaemic state can cause endothelial injury and venous stasis which increases risk for thrombosis as explained by Virchow's traid. Risk for VTE increases by 1.4% among diabetics. Hyperglycemia associated with DM prolongs the state of acute thrombotic inflammation. DM induced hyperglycemia can lead to increased synthesis PAI-1, an intermediary of inflammation. DM is the one the cause for recurrent DVT.

12) Oral contraceptive pills (OCPs) [50]

Women commonly use OCPs for contraception. Use of combined OCPs can cause of DVT among young females. The risk further increases when additional risk aspects are present like obesity, diabetes, trauma, smoking, travel history. In young females, proper evaluation is required before starting OCPs to prevent life threatening condition like pulmonary embolism. The risk for DVT decreases proportionately with the duration and dose of contraceptive pills.

CLINICAL FEATURES [51]

Clinical features can frequently be not much reliable as most of the features can be present due to injury/trauma also. Most often patient don't have any symptoms. Patient may have following clinical features.

1) Erythema

2) Pain

3) Warmth

4) Swelling

CLINICAL SIGNS [52]

1) Homan sign – On dorsiflexion of foot in extended leg patient experiences pain in calf muscles.

2) Moses sign – In this sign, when calf muscles are compressed forward towards the tibia, patient experiences pain.

3) Phlegmasia alba dolens – Edema, discomfort & blanching in absence of cyanosis are the hallmarks of this state.

4) Phlegmasia cerulea dolens – It is categorized by edema, pain & blanching along with cyanosis.

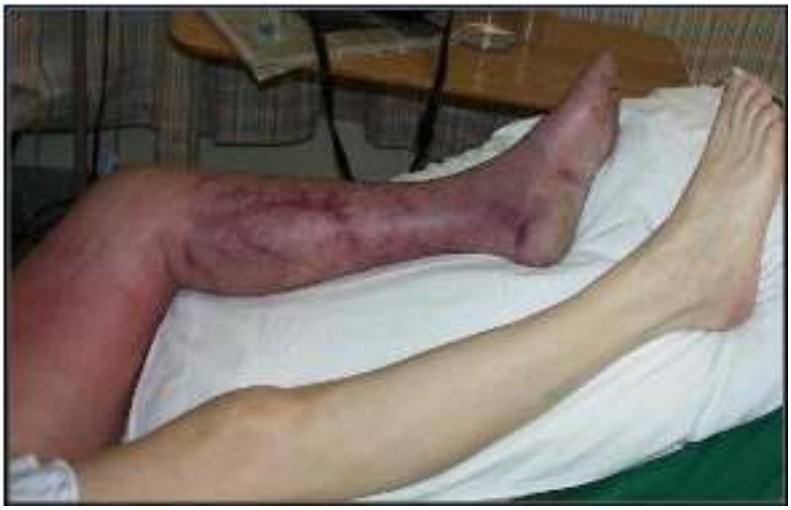


Figure 5: Phlegmasia cerulea dolens

COMPLICATIONS

1) Pulmonary embolism [53]

Recently term VTE is introduced because DVT & PE are co-related to each other. PE carries high mortality. Clinical features of PE include tachycardia, difficulty in breathing and chest pain. Nearly about 90% of symptomatic PE are stated to be originated from thrombi present in deep veins of lower limb. It is evident that around fifty percent of symptomatic patients with DVT can develop PE even after 90 days. So, if we establish DVT well in time, fatal PE can be avoided.

2) Pulmonary hypertension [54]

Chronic Thrombo Embolic Pulmonary Hypertension (CTEPH) is another name for pulmonary hypertension. It is present in 0.1 to 9.1% of patients who recovered from an incident of PE. It can occur even in absence PE. It presents as -

1) Swelling

2) Chest pain

3) Light headedness

4) Breathing difficulties

3) Post thrombotic syndrome (PTS)[55]

PTS is the long-lasting manifestation of DVT. PTS develop in 20-50% patients of DVT. PTS badly affects life of quality. Clinical demonstration of PTS can differ from mild signs to more severe signs like long-lasting leg pain, ulcer formation. Characteristic PTS symptoms are – sensations of heaviness in leg, fatigue and swelling. Typical signs include –redness, stasis, hyperpigmentation, cyanosis and lipodermatosclerosis. Lipodermatosclerosis is abnormal thickening skin along with subcutaneous tissue. In severe cases, it presents as leg ulcers which are severely

painful and are precipitated by minor trauma. PTS develop due to dysfunctional valves leading to elevated venous pressure. Perfusion of calf muscle is reduced and permeability is increased leading to swelling. Leg strengthening exercises and compression therapy can prevent ulceration. Ulcers are often managed using multidisciplinary approach that involves surgeon, dermatologist and nursing care.

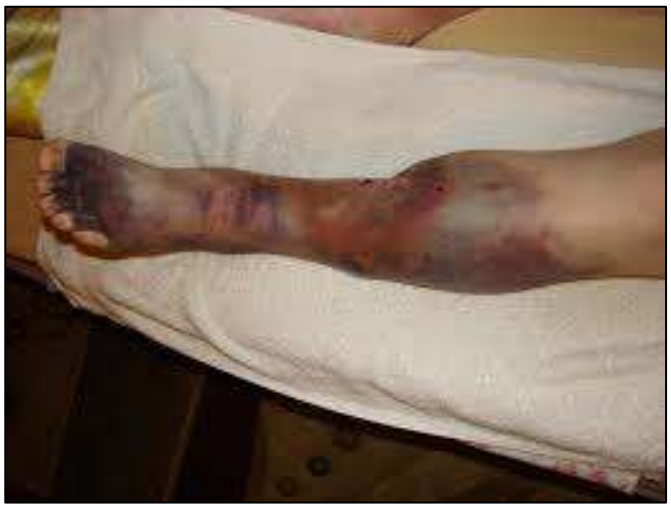


Figure 6: Venous ulceration

Wells prediction rules [56]

Wells designed a score to define probability of which patient can develop DVT. Venous Doppler is the investigation that is used these days for diagnosing DVT, but it is very expensive modality to diagnose. Wells score can outline likelihood of pre-test possibility of DVT, which may guide subsequent investigation and management.

Wells Clinical Prediction Rule for Deep Venous Thrombosis (DVT)

Clinical feature	Points
Collateral superficial veins	**1**
Paralysis/immobilization	**1**
Bedridden for >3 days following surgery	**1**
Localized tenderness	**1**
Paralysis/immobilization	**1**
Calf swelling of >3 cm`	**1**
Unilateral pitting edema	**1**
Malignancy	**1**
Suspecting other alternative diagnosis	**-2**
Total points	

Table 1: Wells criteria for prediction of DVT

Interpretation

Risk score interpretation (probability of DVT):

• =3 points: high risk (75%);

• 1 to 2 points: moderate risk (17%);

• 1 point: low risk (3%).

DIAGNOSTIC TESTS

1) Contrast Venography [57]

It was historically a first imaging technique for diagnosing DVT. It is considered as gold standard to diagnose DVT. Thrombus is recognized as the filling defects or non-opacification in veins. The major setback is that it is invasive nature which requires medical expertise. Anaphylactic reactions have been noted because this involves the usage of dye. With new imaging modalities this method to diagnose DVT is infrequently used these days.

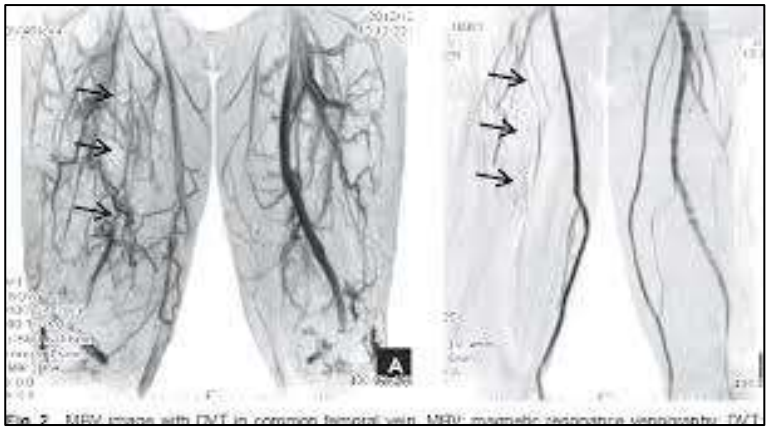


Figure 7: Contrast venography

2) Venous ultrasound [58]

Its various benefits like low cost, non-invasive nature, easy availability make it investigation of choice for diagnosing DVT. There are 3 kinds of venous USG

1) Compression USG
2) Duplex USG
3) Isolated Color doppler USG

Compression USG is generally used for proximal veins. Combination of color and duplex ultrasound is done for calf & iliac veins. The major criterion of DVT is the absence of compression of lumen of vein with gentle pressure applied by probe. Other criteria involve nonappearance of pattern in which blood flows & absence of colour or spectral signals from vein lumen.

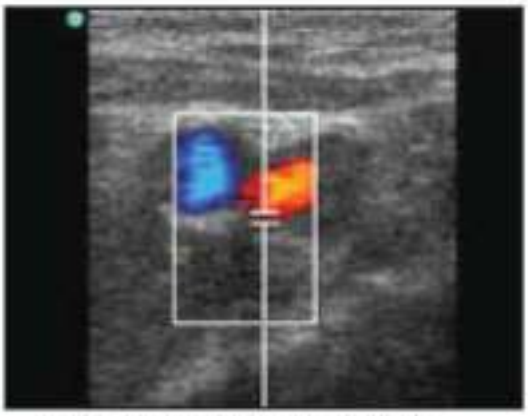
Advantages-

1) It can diagnose various other pathologies like femoral aneurysm, lymphadenopathy, Baker's cyst, intramuscular hematoma, abscess, superficial thrombophlebitis.
2) Non-invasive so there no chances of infections and bleeding
3) Easy availability

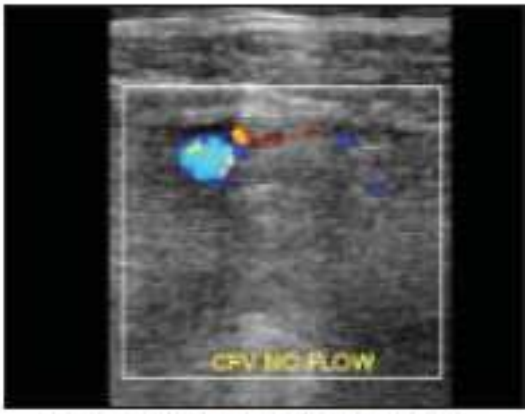
Limitations

1) The major drawback of venous USG is that venous compression is determined by patient's characteristics like obesity, oedema, tenderness, splints, casts application.
2) It requires medical expertise.
3) Expensive.
4) It is an operator dependent procedure. So interpretation can be subjective.

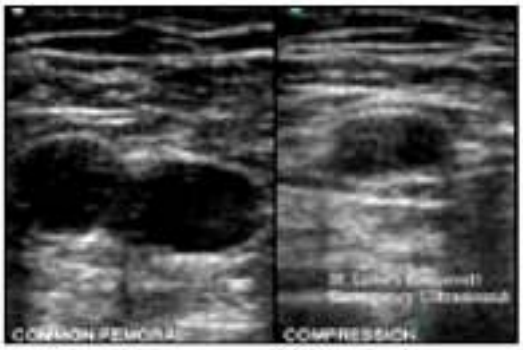
The sensitivity & specificity of B mode ultrasonography is 95 % and 96 % respectively.



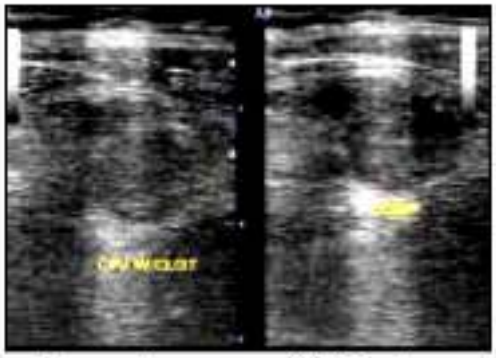
Color-flow Doppler in normal vessels.



Color-flow Doppler in deep vein thrombosis.



Normal compressibility of the common femoral vein.



Abnormal compressibility in deep vein thrombosis.

3) Impedance plethysmography [58,59]

Cuff is inflated over the thigh for occluding the venous circulation resulting in accumulation of blood in venous system resulting in decrement in the impedance. The abrupt release of cuff will lead to rapid increase of impedance. Obstruction of vein as in DVT will lead to reduction in rate of venous drainage (slower increase of impedance in venous system) as compared to normal. This investigation is operator dependant and need expertise so sensitivity is considered low in some studies.

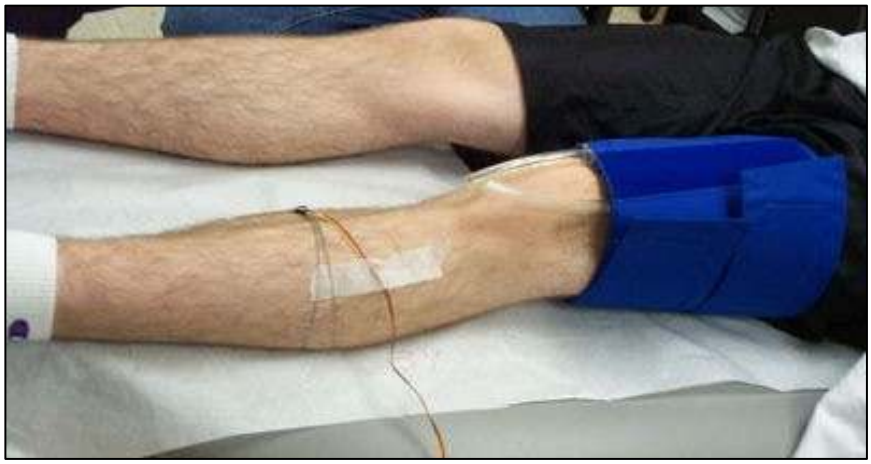


Figure 8: Impedance plethysmography

4) Role of D-dimer levels[60]

D-dimer is the degradation products of fibrinogen. Fibrinogen is the glycoprotein, which might be transformed via thrombin to fibrin throughout blood clot establishment. D-dimer value measurement is very useful in non-traumatic cases. In fractures/trauma, levels of D-dimer will be drastically elevated due to continuous process of clot development and degradation.

DVT PREVENTION:

DVT prevention can be classified under 3 headings:

1) Primary prevention
2) Physical prevention
3) Pharmacological prevention

Primary Prevention

1) Surgical techniques – Respecting soft structures and causing minimal damage to vessels. Injury to walls of vessels leads local inflammatory response causing activation of coagulation.

2) Standardization of timing for tourniquet application.

3) Prevention of dehydration – Administration of adequate fluids pre & post operatively. Patients must be encouraged to stay hydrated.

4) Early mobilization – Early Mobilization after surgeries can prevent DVT. Mobilization will cause effective activation of calf muscular pump mechanism preventing venous sluggishness.

5) Life style modification – Patients must be encouraged to adopt healthy life style which include weight loss, stop smoking, and maintain healthy weight & good control of sugars.

Physical preventive measures

1) Use of compression elastic stockings.
2) Pneumatic compression devises.

These methods will prevent venous stasis and cause degradation of thrombi and embolus by activating fibrinolytic system of endothelium.

Compression elastic stockings [61]

Compression produced by applying elastic stockings can upsurge the drainage of blood in veins. It is applied either till thigh length or calf length. It is cost-effective method of preventing DVT.

Advantages – easy to use, cost effective, no risk of bleeding or infections, easily available

Limitations – certain skin conditions like dermatitis, cardiac patients, arterial occlusive diseases limit its use

Intermittent Pneumatic compression [62]

It is proven method to prevent DVT after orthopaedic surgeries. It comprises of pneumatic garment, compressor to intermittently cause compression.

Garments- for prophylactic purpose of DVT single use garments are administered to decrease chances of infections. Different garment sizes are available. All intermittent compression devices use intermittent pressure. They contain air bladders. Garments are circumferential or non- circumferential. Circumferential garments will encase whole limb in contrast to non-circumferential garment which will compress along the part of circumference of limb.

Pumps: They can either be battery driven or electrically powered.

Pressure

40 mmhg is the average pressure applied

Applications

1) Arterial disease
2) Lymphedema
3) Venous insufficiency
4) DVT Prophylaxis

Adverse effects

1) Skin irritation
2) Ulcer formation
3) Palsy of peroneal nerve

Contraindications

1) Dermatological manifestations like cellulitis, infections
2) Massive edema
3) Established DVT

Limitations

1) Poor compliance of patients
2) Regular monitoring is needed
3) Have to educate patient about use

Pharmacological approaches of prophylaxis

Aspirin [63]

Aspirin works by inhibiting an enzyme known as cyclooxygenase thus inhibiting production of thromboxane. This enzyme is irreversible & action lasts for 7-10 days. It is orally administered drug. Aspirin in small doses is safe & efficient

way to prevent DVT. There is reduction in incidence of DVT with aspirin after orthopaedic surgeries.

Vitamin K antagonist[64]

Mechanism – It acts by inhibiting gamma carboxylation of glutamate residues present at N terminal of proteins which are vitamin k dependent thereby inhibiting cyclic alteration of vit K thereby inhibiting production of vit K dependent clotting factors.

Two commonly available drugs are

1) warfarin
2) Acenocoumarol

$T_{1/2}$ of warfarin is 2-3 days and half-life of acenocoumarol is around 10 hours. PT should be closely checked whenever patient is on these drugs. PT test uses a value called as INR. The normal INR level is 2-3 with target value of 2.5 when patient is on warfarin. INR should be monitored after 2-3 days of initiation of warfarin. Once the desired levels of INR are reached, after that once in 4 weeks it is recommended. Warfarin takes around 3 -4 days to reach desired INR values. For first 3 -4 days warfarin should be given along with LMWH.

Advantages

1) Oral administration
2) Easy availability

Disadvantages

1) Risk of internal breeding
2) Skin necrosis caused by warfarin
3) Drug interactions
4) Requires regular laboratory monitoring

Unfractionated heparin (UFH) [65]

Unfractionated heparin consists of heterogeneous combination of glycosaminoglycans. Mechanism of action – UFH acts via its pentasaccharide sequence and fixes to antithrombin (AT) which leads in deactivation of thrombin & various other clotting factors like factor 2a, 9a, 11a, 12a. Route of administration- it is taken either via subcutaneous route or via continuous intravenous infusion. Heparin is not absorbed via oral route. ACCP recommends regular use of heparin as a prophylactic agent to prevent VTE/DVT after major orthopaedic surgeries. Effect of heparin is measured by a lab value known as aPTT.

Limitations

1) Requires lab monitoring of aPTT
2) Bleeding
3) Cannot be administered orally
4) Skin necrosis
5) Thrombocytopenia
6) Chronic use of heparin leads to osteoporosis and osteopenia

Newer agents

There are certain limitations with conventional anticoagulants. These limitations are as follows-

1) Subcutaneous administration
2) Laboratory monitoring is required
3) Risk for thrombocytopenia
4) Bleeding

So, the newer agents like Rivaroxaban are introduced to overcome the limitations of conventional anticoagulants.

Rivaroxaban [66]

It acts by directly inhibiting factor Xa. It is currently suggested in TKR and THR patients. It is administered orally. Dose for prophylaxis is 10 mg as a fixed oral dose for THR and TKR. Major advantage is it doesn't require lab monitoring. Its efficacy after hip fractures has not been studied widely so ACCP doesn't recommend its use after hip surgery. Studies have shown it more efficacious than LMWH and UFH for prophylaxis after TKR and THR.

Contraindications of anticoagulants

Contraindications of anticoagulants are as follow

1) Platelet count less < 1 lakh
2) Active bleeding
3) Patient having thrombocytopenia with usage of heparin
4) Patients having allergic reactions to use of heparin
5) Patients not complaint for lab monitoring
6) Intracranial haemorrhage/aneurysms
7) Inherited thrombophilia

Role of thrombolysis [67]

It is specified for conditions like pain in involved limb, swelling in limb, ulceration and functional disability. Thrombolytic drugs are delivered via catheter - based techniques. The plus point is very large amount of these drugs can be attained locally, leading to very little systemic adverse reactions of fibrinolytic agents. After successful lysis of clot, veins are evaluated by venography to check successful elimination of thrombus and if any residual thrombus is left that are removed by either placing stents or with balloon angioplasty. The major drawback is requirement of

long infusion time to lyse thrombus. Anticoagulants should be used before & after the completion of procedure. If patient is having active bleeding secondary to any reason like surgeries, CRF patients, intracranial bleeding we should be very cautious using these agents. Urgent thrombolysis should be done in case there is threat to limb and there is high risk for fatal PE. Thrombus formation in common iliac veins & femoral veins are at very high risk for deadly PE.

IVC filters [68]

Filters of IVC are the mechanical devices which are inserted through percutaneous route under image supervision. They are used when patients are more predisposed to a medical condition known as PE and in whom anticoagulants are not suggested. They are accessible in two possibilities permanent filters or optional filters. The major modification between permanent filters and optional filters is temporary filters can be retrieved after sometime. Contraindications for the administering anticoagulants comprise of active bleeding, inherited thrombophilia, anticoagulant induced thrombocytopenia, intracranial hemorrhage, severe renal disorders, hepatic dysfunction. Failure of anticoagulation is also classic indication for IVC filters.

TREATMENT OF DVT[68]

The main aim to treat DVT is to prevent both acute and chronic complications of DVT. Acute complication includes extension of thrombus and acute PE. Chronic complications include post thrombotic syndrome and chronic pulmonary hypertension.

Initial treatment includes achieving therapeutic levels of un-fractioned heparin or low molecular weight heparin. Studies have shown that the efficacy of treatment with heparin largely depends on the ability to achieve a critical therapeutic ratio

within the first 24 hours of treatment. LMWH is preferred in treatment of acute DVT and PE over UFH because of its various advantages, however UFH is given in patients of chronic renal failure patients because LMWH is excreted via kidneys. Heparin is initially given with warfarin and stopped after a minimum of 4 to 5 days, during which international normalized ratio (INR) is maintained within 2.0 to 3.0 (therapeutic range). This overlap with warfarin is essential because factors II, IX, X will not be affected until after 5 days, hence the intrinsic clotting pathway will be intact.

Warfarin remains drug of choice for long term management once the acute anticoagulation has been achieved. LMWH is drug used for long term management in pregnancy as warfarin is contraindicated in pregnancy. LMWH is more effective than warfarin in preventing recurrent thrombosis.

3-month duration of treatment is recommended in case thrombosis is at proximal veins of lower limb and in whom risk factors are transient like surgery and trauma as chances of development of recurrent thrombosis is rare.

Long duration of treatment is recommended in patient where ongoing risk factors are present like malignancy, post thrombotic syndrome, unprovoked episode of PE, elevated antiphospholipid antibodies.

New drug like apixaban is recommended in the dose 10 mg two times a day for first seven days than 5 mg once a day. Rivoxaban is given in the dose of 15 mg twice a day for first 21 days followed by 20 mg once a day. Dabigatran is given in the dose of 150 once a day for the duration of treament. The advantage of using these drugs are lab monitoring is not required and can be orally administered.

Thrombolytic therapy indicated in massive DVT which leads to phlegmasia cerulean dolens and threatened limb loss. The available thrombolytic agents include tissue plasminogen activator, streptokinase, and urokinase.

Vena cava filters are indicated in few circumstances. They are used when there is absolute contraindication to anticoagulation therapy like life-threatening haemorrhage on anticoagulation, and failure to achieve adequate anticoagulation.

MATERIALS AND METHODS

Material and methods

The present study was conducted in KLES Dr Prabhakar Kore hospital and medical Research centre, Belagavi after obtaining the ethical committee approval.

Study Design

Hospital based 1 Year observational study

Study period – 1st January-31st December 2020

Source of data

Patients undergoing major orthopaedic surgeries orthopaedics department at the KLES DR. Prabhakar Kore hospital and medical Research Centre, Belagavi in between 1st January 2020 to 31st December 2020, over a period of one year.

Sample size

Formula used for sample size calculation was

$$n = \frac{(100-p)Z^2}{E_2}$$

n was sample required, **p** was the percentage existence of state or condition (proportion or prevalence), **E** was the percentage maximum error required, **Z** was the value corresponding to level of confidence required.

As there was DVT incidence of 19.6% in one of the study researches from India[23], this incidence was applied to calculate sample size. With 90% confidence level and 10% maximum error, sample size required is,

$$n = \frac{19.6 \times (100 - 19.6) \times (1.64)^2}{10_2}$$

$$n = 42.38 \approx \mathbf{42}$$

Hence sample size required was 42

Data analysis

Data was analyzed using statistical software **R version 4.0.2** and **Microsoft Excel**. Continuous variables represented by mean± sd/median (range) and categorical variables represented by frequency and percentage. To check the association between categorical variables Chi-square test is applied. For comparison mean/distributions between groups t-test/Mann-Whitney test is used. P-value less than or equal to 0.05 indicates statistical significance.

Selection criteria:

Inclusion criteria:

1) Patients who gave their willfull consent for participation in study
2) Age >18 years
3) Fractures that need surgical treatment;
4) Hospitalization of minimum of 5 days

Exclusion criteria:

1) Any haematological disease
2) Patients having any malignant condition
3) Patients having DVT in past
4) Patients on anticoagulants
5) Female patients on OCPs
6) Pathological fractures
7) Isolated upper limb fractures
8) Patients having pre-operative DVT

Procedure

Purpose of study was explained to all and written consent was taken from all in their own vernacular language.

Patients underwent colour Doppler USG both pre-operatively and post-operatively. Post operatively colour Doppler was performed on post-operative day 5. Patients were operated according to nature of the fracture. Patients were evaluated during hospital stay for signs & symptoms.

Data collection using proforma

Patients were assessed through proforma & after ruling out the patients in the exclusion criteria & inclusion criteria.

OPD No: To maintain records

Name: For identification of patients and to maintain medical records

Age: Age is vital factor, as the study was focused to know at which age DVT is more prevalent.

Sex: Both Males and Female were included.

Address: Address was noted to communicate with patient

Socioeconomic Status: Was classified into upper, middle and lower status based on income.

Questionnaire:

1. Mechanism of trauma:

   Mode of trauma was asked to each subject to judge fracture type and associated injuries

2. Medication History:

3. For ruling out exclusion norms. Medication history about blood thinners, anti - cancer medication, diabetic medications, medications for cardiac diseases

History suggestive of following chronic diseases:

a. Chronic liver disease

b. CKD

c. Skin diseases

d. Rheumatoid arthritis

e. Hypertension

f. Malignant conditions

1) H/o alcohol Consumption.

H/o alcohol intake was asked to know if alcohol consumption is risk factor for development DVT

2) Habit of smoking cigarettes.

Cigarette smoking was asked to evaluate if smoking is risk aspect. If the patient smoked cigarettes, the no. Of cigarettes smoked per day was noted.

3) BMI was calculated after determining the Height & weight

BMI: - wt(kg)/Ht(m2)

4) Blood pressure

Investigations:

1. Random blood glucose levesl
2. Creatinine levels
3. D Dimer levels
4. Lipid levels
5. Highly specific C reactive proteins
6. Colour venous Doppler study of fractured lower limb pre-operatively and post operatively
7. Required X Rays

Colour Doppler Evaluation technique:

This was performed in supine position after removal dressings, cast and slab. Procedure was non-invasive and was accomplished in about 30 mins. The major criteria was inability to compress the lumen of vein with moderate pressure with probe. Other criteria involve absence of pattern in which blood flows and absence of color or spectral signals from vein lumen.

Pre-Scan Requisites

1. Completion of the questionnaire
2. Selection of study group after inclusion & exclusion
3. Filling of the informed consent.

RESULTS

In our study, there were 42 subjects, with age of 51.12±20.09 years. There were 15 females and 27 males in the study. Among 42 fractures 18 were hip fractures, 10 were tibia shaft fractures, 2 were ankle fractures, 7 were femur shaft fractures, 4 fractures were around knee joint and 1 had pelvic fracture. Post operatively 9 subjects had DVT. Among 9 DVT subjects 6 had fractures around hip joint, 1 had femur shaft fracture, 1 fracture around knee joint, 1 had pelvic fracture. DVT incidence after major orthopaedic surgeries was determined to be 21.4%. Smoking, alcohol intake, diabetes mellitus, BMI >25 were the risk factors for development of DVT. Out of 9 DVT patients, 7(77.78%) were smokers (p value of 0.0004), 6 had history of alcohol consumption (p value 0.001), 7 (77.78%; p value 0.0004) were diabetics, and 8 (88.89%; p value 0.001) had BMI >25.

Table 2: Summary of variables

Variables	Sub-category	Number of subjects (%)
Age (in years)	≤ 30	12 (28.57%)
	31-40	4 (9.52%)
	41-50	2 (4.76%)
	51-60	7 (16.67%)
	61-70	9 (21.43%)
	71-80	6 (14.29%)
	≥ 81	2 (4.76%)
Age (in years)	51.12±20.09	51.45 (21, 87)
Sex	Female	15 (35.71%)
	Male	27 (64.29%)
Smoking	No	31 (73.81%)
	Yes	11 (26.19%)
Alcohol	No	33 (78.57%)
	Yes	9 (21.43%)
DM	Absent	33 (78.57%)
	Present	9 (21.43%)
HTN	Absent	30 (71.43%)
	Present	12 (28.57%)
BMI (Kg/m^2)	< 25	24 (57.14%)
	≥ 25	18 (42.86%)
BMI (Kg/m^2)	24.21±2.83	24 (19, 29)
Diagnosis	Fractures around Hip joint	18 (42.9%)
	Fractures femur shaft	7 (16.67%)
	Fractures around Knee joint	4 (9.52%)
	Fractures Tibial Shaft	10 (23.81%)
	Fractures around Ankle joint	2 (4.76%)
	Fractures around Pelvis	1 (2.4%)
Type Of Operation	CRIF with IMIL	27 (64.29%)
	ORIF with plating	5 (11.9%)
	Tension band wiring	1 (2.38%)

	Hemiarthroplasty	5 (11.9%)
	External fixation with external fixator/LRS	3 (7.14%)
	ORIF with DHS	1 (2.38%)
Pre-Operative Doppler Evaluation	Normal Doppler Study	40 (95.24%)
	Superficial Thrombophlebitis	1 (2.38%)
Post-Operative Doppler Evaluation	Deep Vein Thrombosis	9 (21.43%)
	Normal Doppler Study	32 (76.19%)
	Varicose Veins	1 (2.38%)
Pre-operative-D Dimer	612.86±311.77	548 (121, 1160)
Post-operative D-Dimer	1016.5±364.11	1200 (100, 1499)
Pre-operative HsCRP	46.77±63.25	34 (1.5, 350.4)
Post-operative HsCRP	81.41±45.24	65.3 (8.9, 184)
Cholesterol levels	130.55±26.69	125 (89, 204)
Creatinine	0.9±0.21	0.88 (0.52, 1.48)
Platelet counts	263.21±61.45	256.5 (123, 365)
RBS	107.31±36.1	95 (10, 199)

Below plot visualizes the above table.

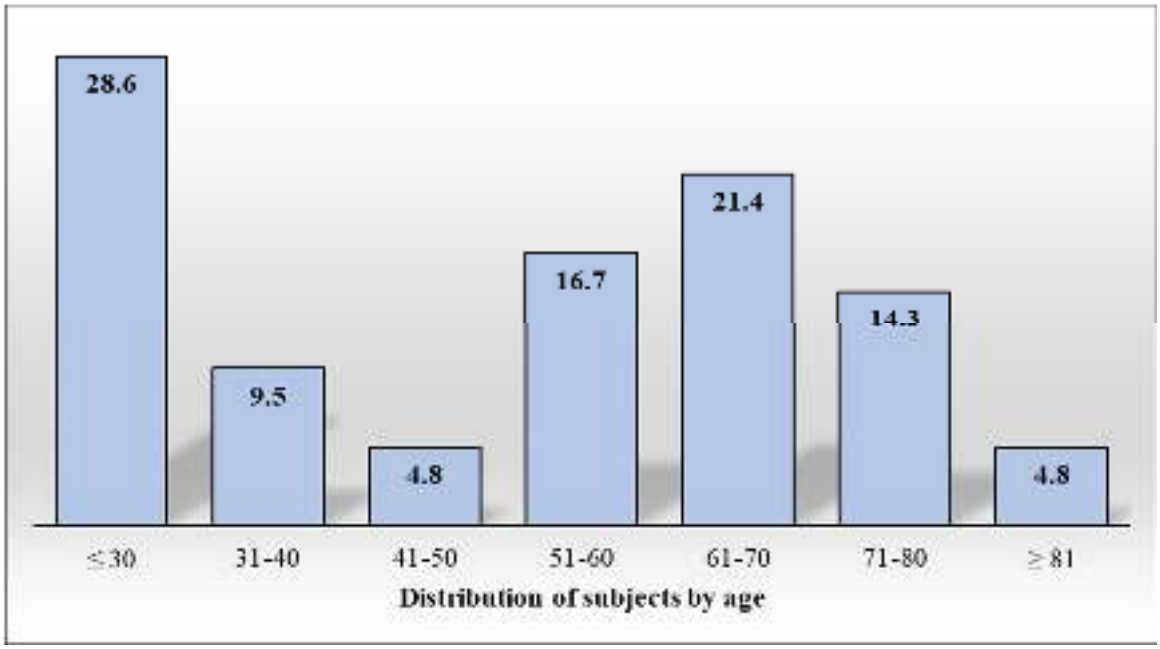


Figure 9: Distribution of subjects by age

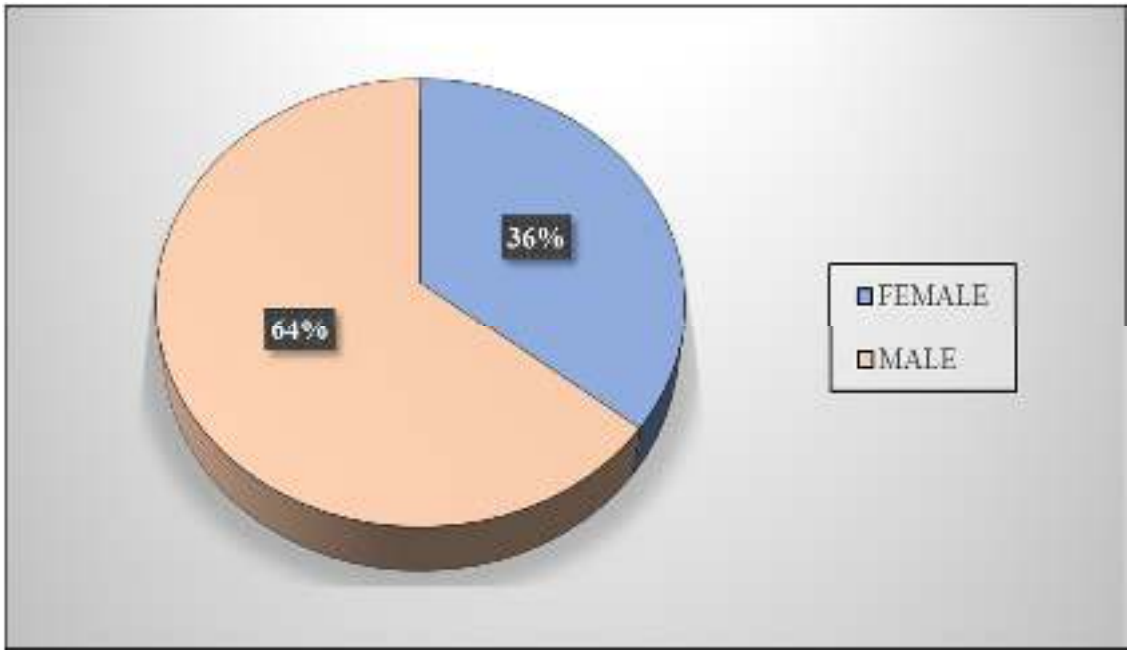


Figure 10: Distribution of subjects by gender

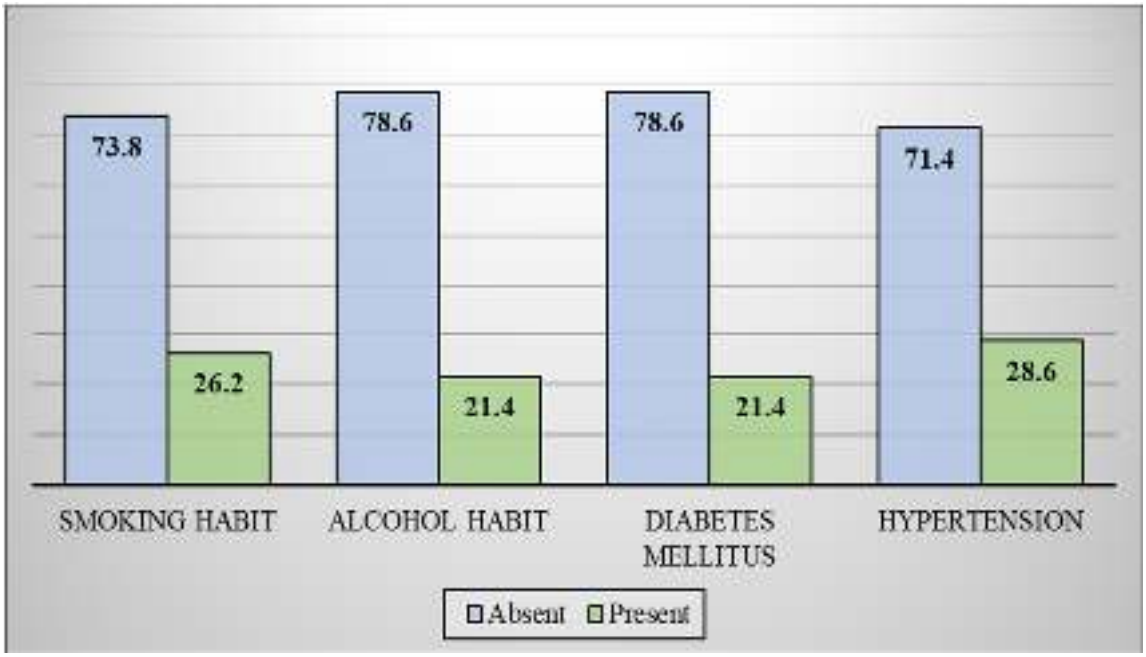


Figure 11: Distribution of subjects by habits and comorbidities

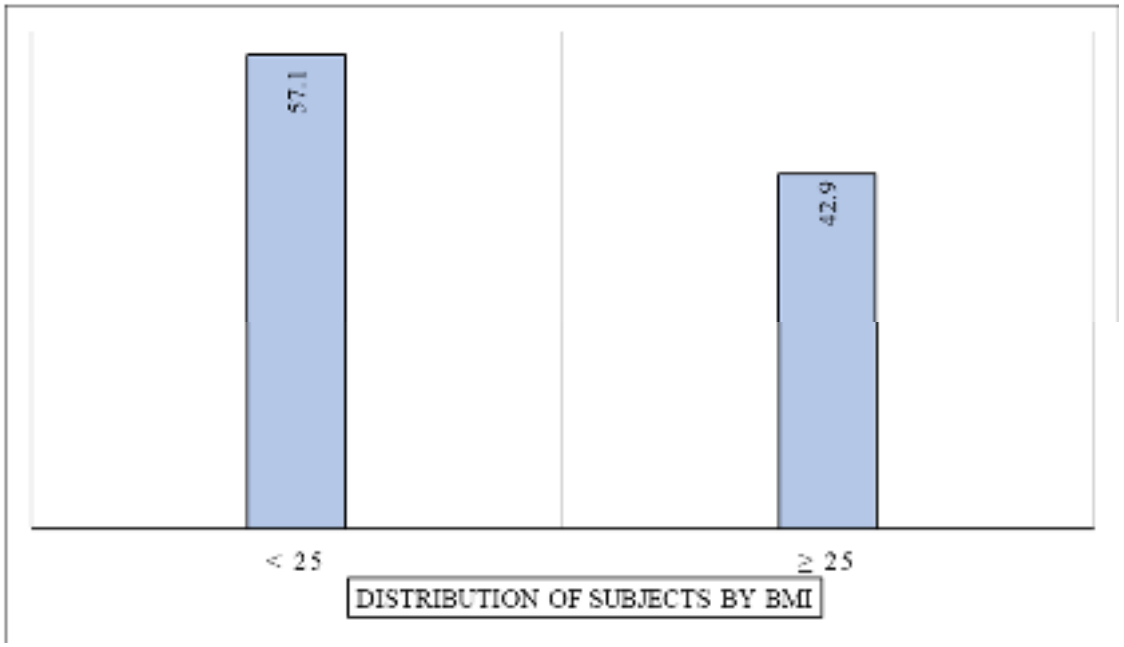


Figure 12: Distribution of subjects by BMI category

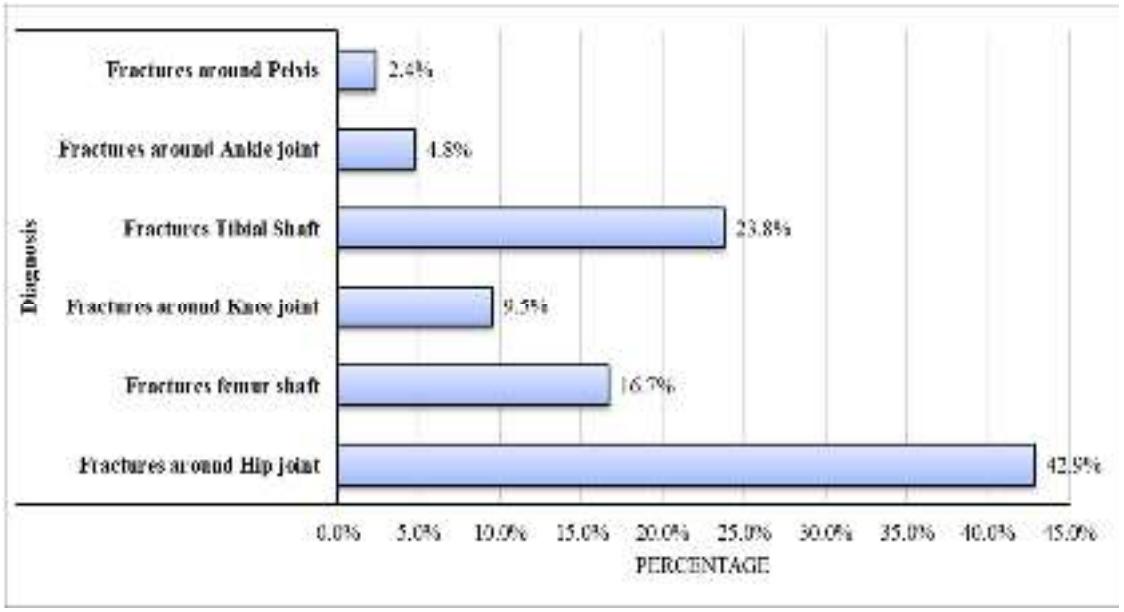


Figure 13: Distribution of subjects by diagnosis

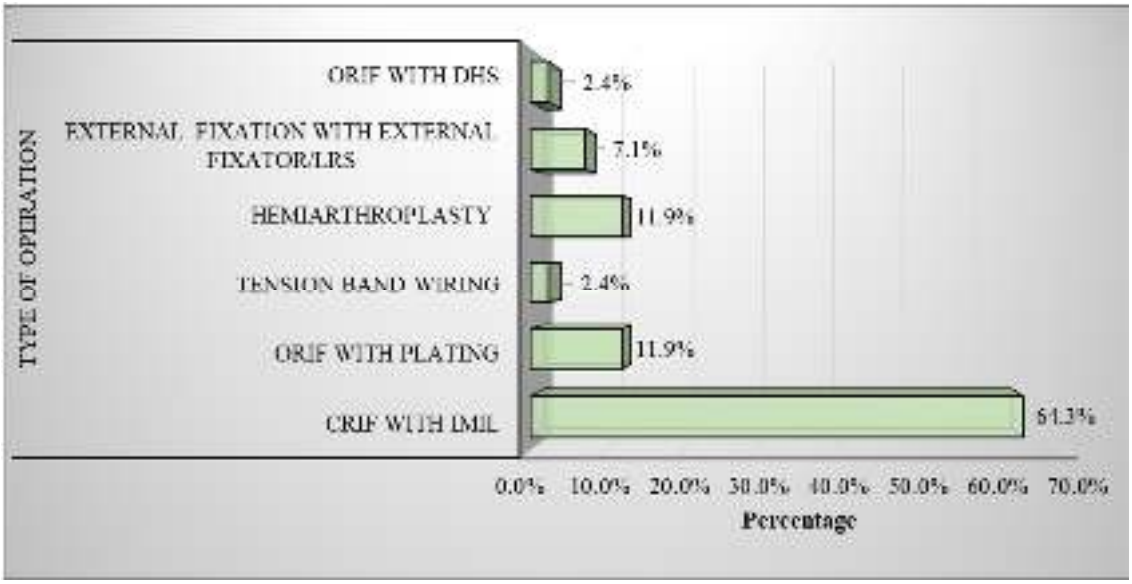


Figure 14: Distribution of subjects by type of operation

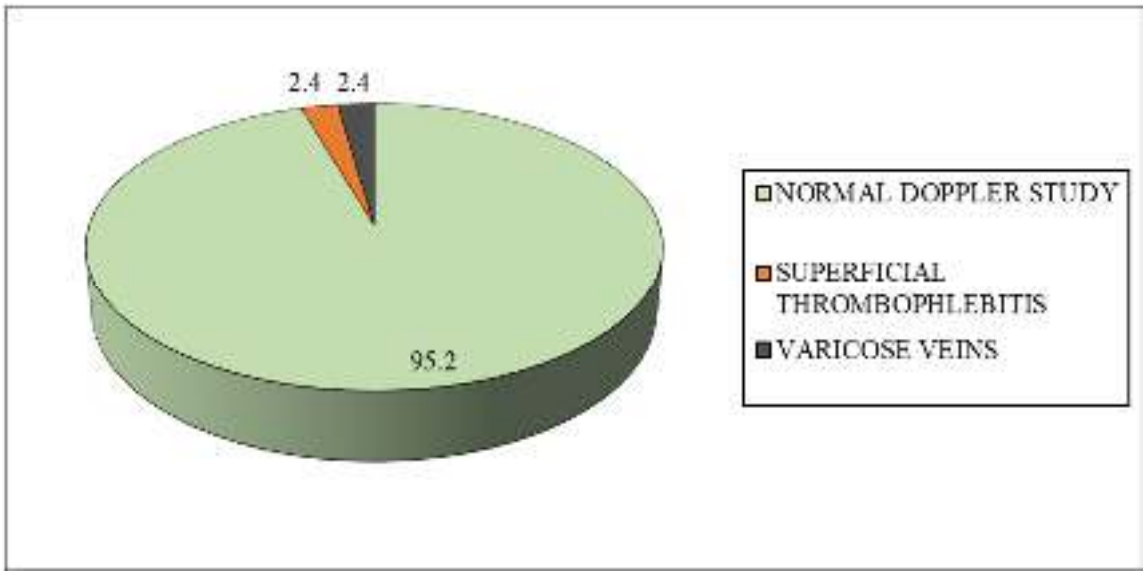


Figure 15: Distribution of subjects by pre-operative Doppler study.

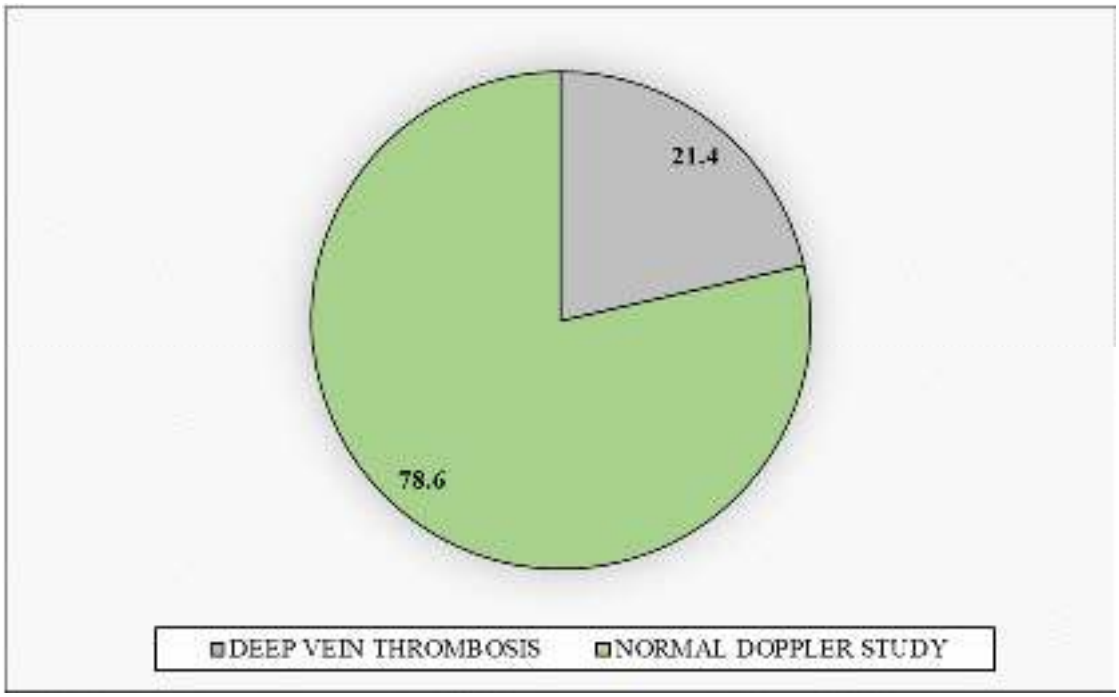


Figure 16: Distribution of subjects by post-operative Doppler study.

Below table compares the parameters over DVT.

Table 3: Comparison of parameters over DVT.

		Post-operative Doppler		p-value
		DVT	**Normal**	
Age (in years)	≤ 30	1 (11.11%)	11 (33.33%)	0.2624[MC]
	31-40	0 (0%)	4 (12.12%)	
	41-50	1 (11.11%)	1 (3.03%)	
	51-60	1 (11.11%)	6 (18.18%)	
	61-70	3 (33.33%)	6 (18.18%)	
	71-80	3 (33.33%)	3 (9.09%)	
	≥ 81	0 (0%)	2 (6.06%)	
Age (in years)		61±15.51	48.42±20.54	0.0963 [t]
Sex	Female	4 (44.44%)	11 (33.33%)	0.6722[MC]
	Male	5 (55.56%)	22 (66.67%)	
Smoking	No	2 (22.22%)	29 (87.88%)	0.0004998*[MC]
	Yes	7 (77.78%)	4 (12.12%)	
Alcohol	No	3 (33.33%)	30 (90.91%)	0.0009995*[MC]
	Yes	6 (66.67%)	3 (9.09%)	
DM	Absent	2 (22.22%)	31 (93.94%)	0.0004998*[MC]
	Present	7 (77.78%)	2 (6.06%)	
HTN	Absent	2 (22.22%)	28 (84.85%)	0.0004998*[MC]
	Present	7 (77.78%)	5 (15.15%)	
BMI (Kg/m^2)	< 25	1 (11.11%)	23 (69.7%)	0.001499*[MC]
	≥ 25	8 (88.89%)	10 (30.3%)	
BMI (Kg/m^2)		27.64±1.61	23.28±2.33	<0.00001*[t]
Cholesterol		141.78±37.07	127.48±22.89	0.1568 [t]
Creatinine		0.84±0.23	0.91±0.21	0.411 [t]
Platelet		291.56±49.99	255.48±62.65	0.1197 [t]
RBS		117.11±35.71	104.64±36.29	0.3646 [t]

Abbreviations: MC: Monte-Carlo's simulation; t: t-test

By Chi-square test, there is no substantial difference in the distribution of age, gender over post-operative Doppler.

By Chi-square test, there is significant association present between smoking habit, alcohol consumption, DM, Hypertension and BMI category with post-operative Doppler.

By one tailed two sample t-test, mean of BMI is significantly more for the subjects who had DVT compared to the subjects who are normal.

By two sample t-test, there is no substantial difference in the mean of age, cholesterol, serum creatinine, platelet, RBS over post-operative Doppler.

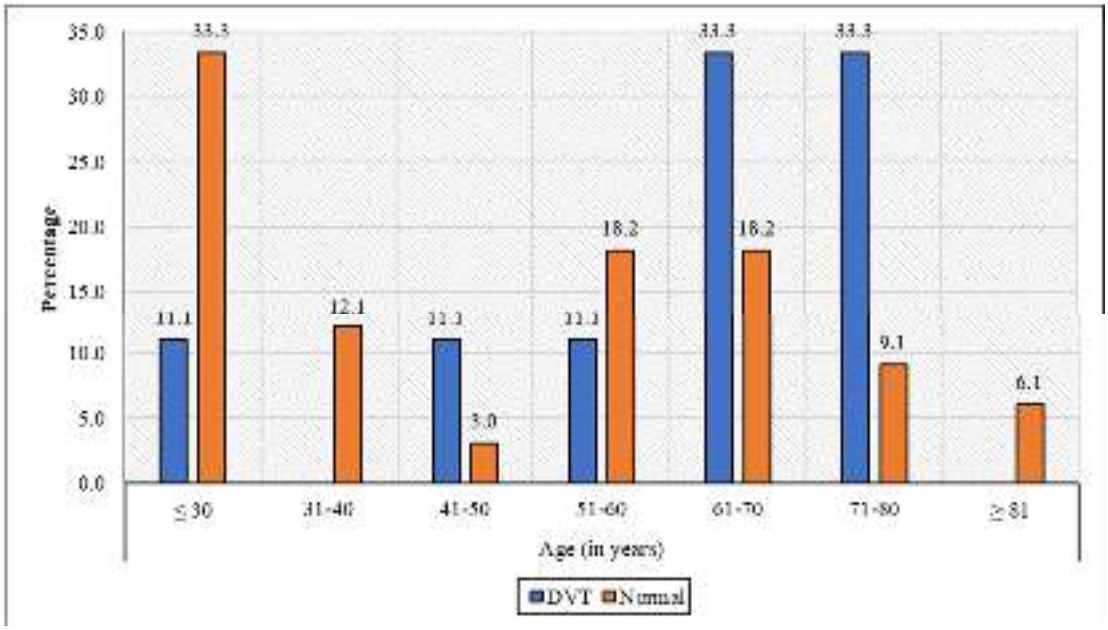


Figure 17: Distribution of subjects by age and post-operative Doppler study.

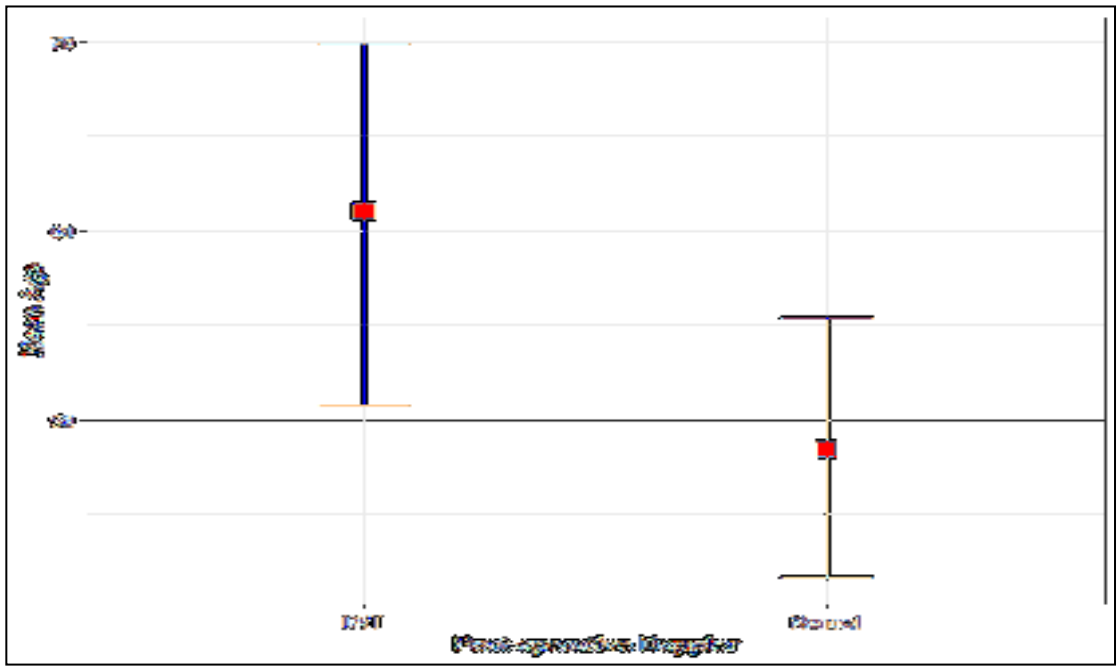


Figure 18: Mean of age by post-operative Doppler study.

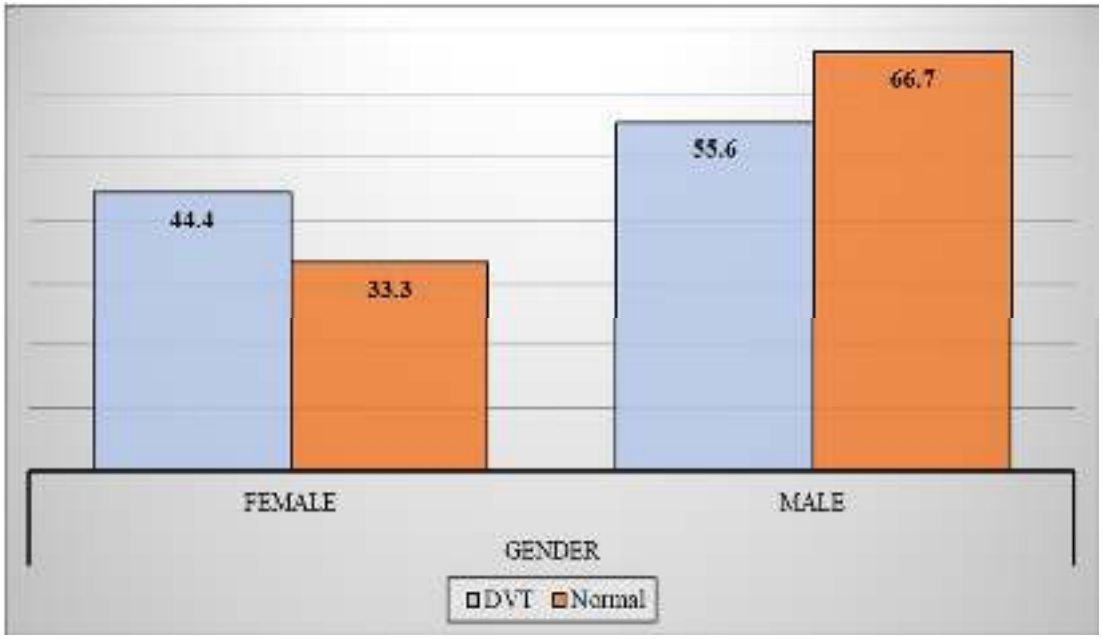


Figure 19: Distribution of subjects by gender and post-operative Doppler study.

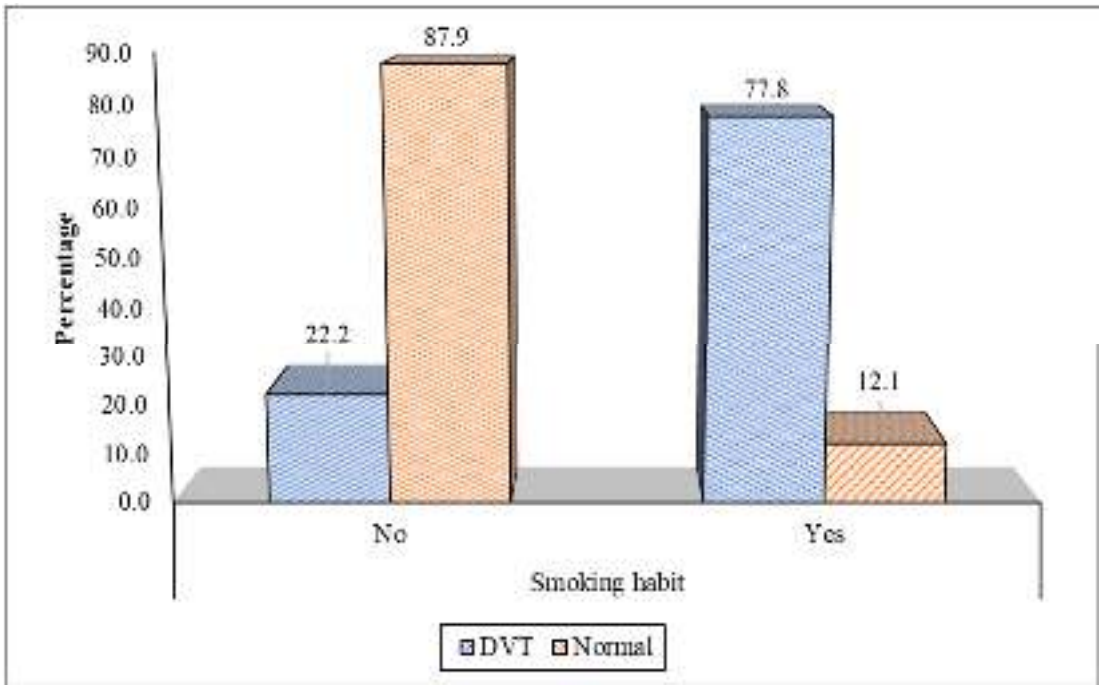


Figure 20: Distribution of subjects by smoking habit and post-operative Doppler study.

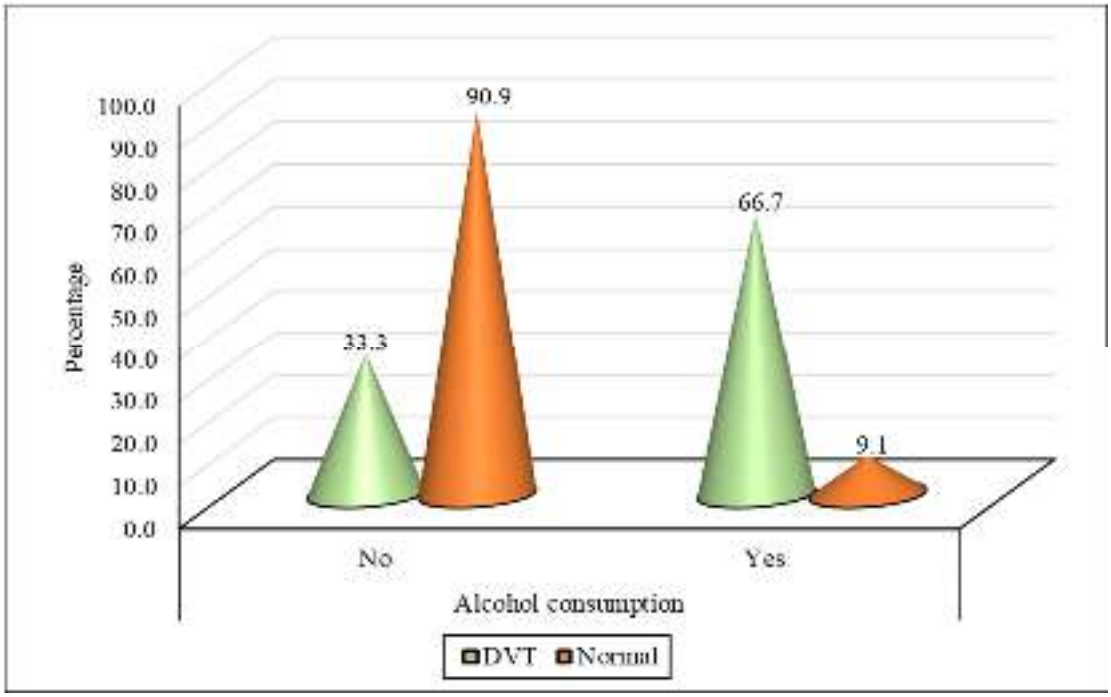


Figure 21: Distribution of subjects by alcohol consumption and post-operative Doppler study.

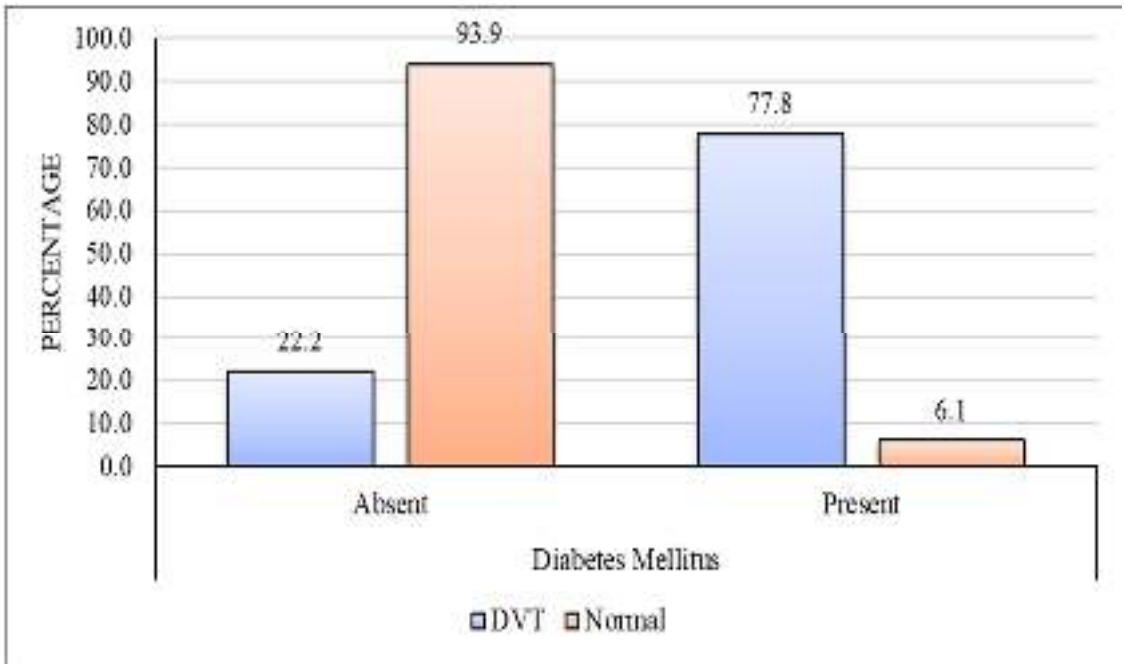


Figure 22: Distribution of subjects by DM and post-operative Doppler study.

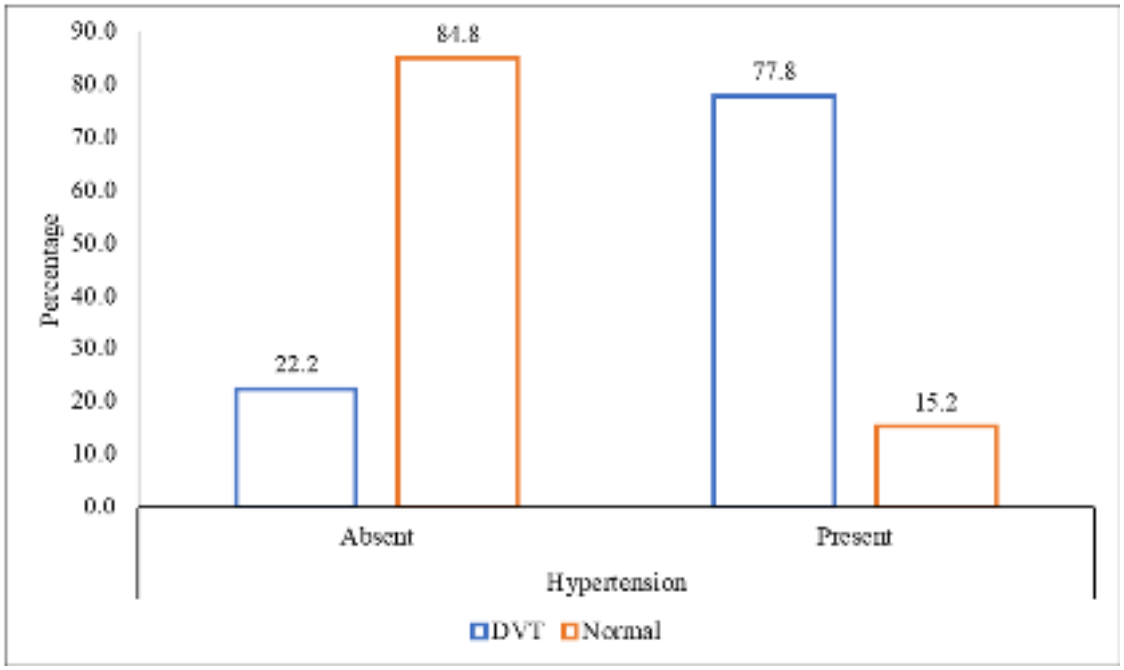


Figure 23: Distribution of subjects by hypertension and post-operative Doppler study.

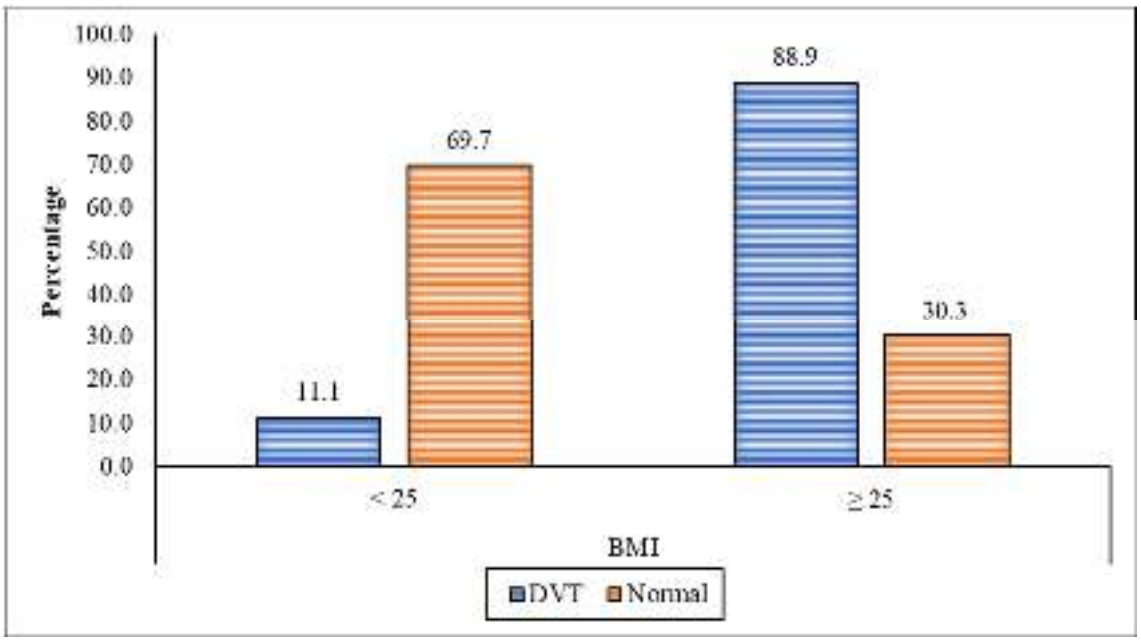


Figure 24: Distribution of subjects by BMI category and post-operative Doppler study.

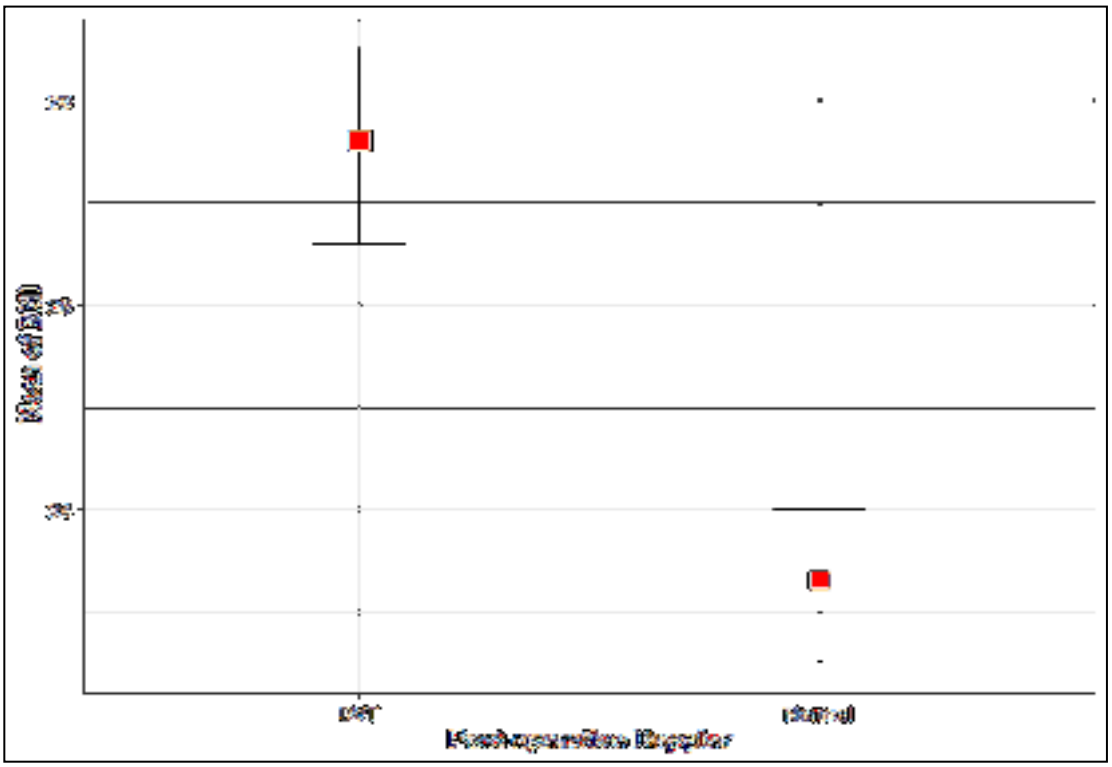


Figure 25: Mean of BMI over post-operative Doppler study.

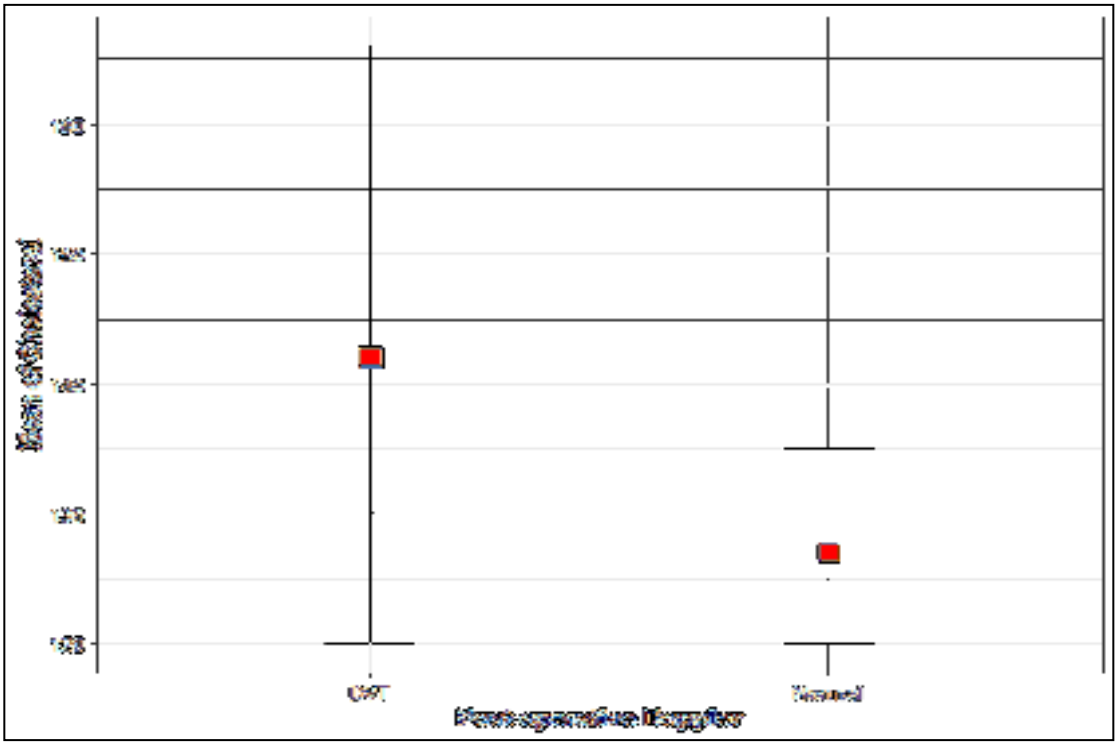


Figure 26: Mean of Cholesterol over post-operative Doppler study.

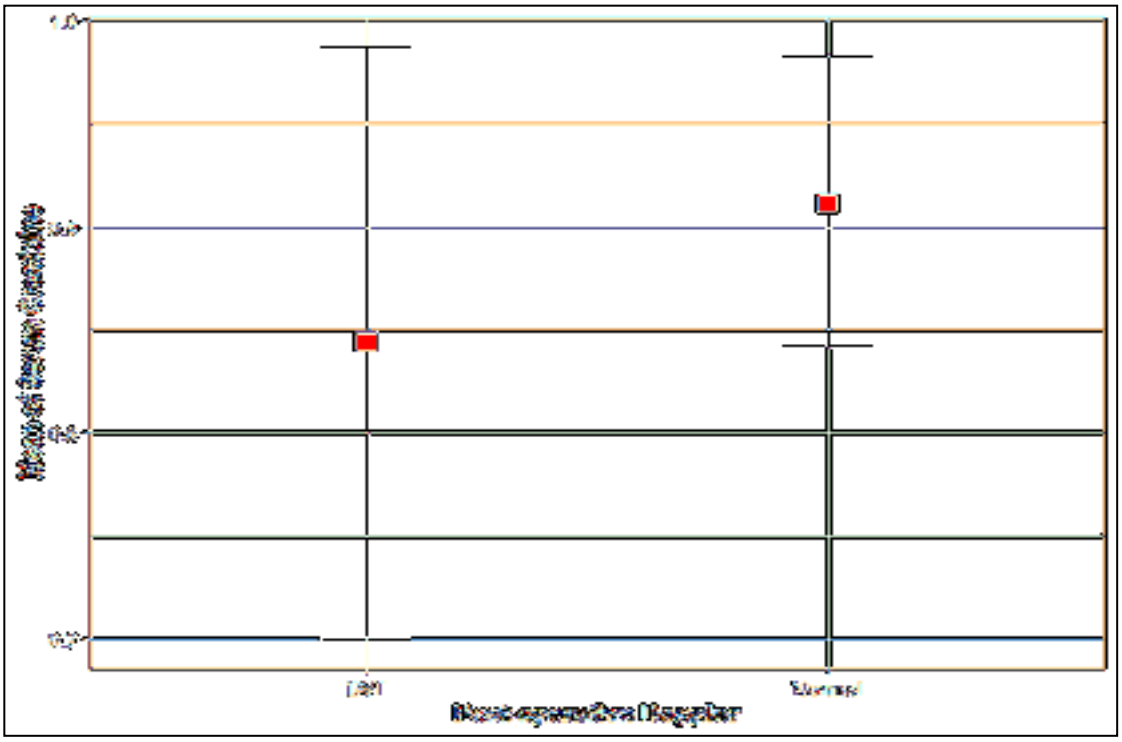


Figure 27: Mean of Serum Creatinine over post-operative Doppler study.

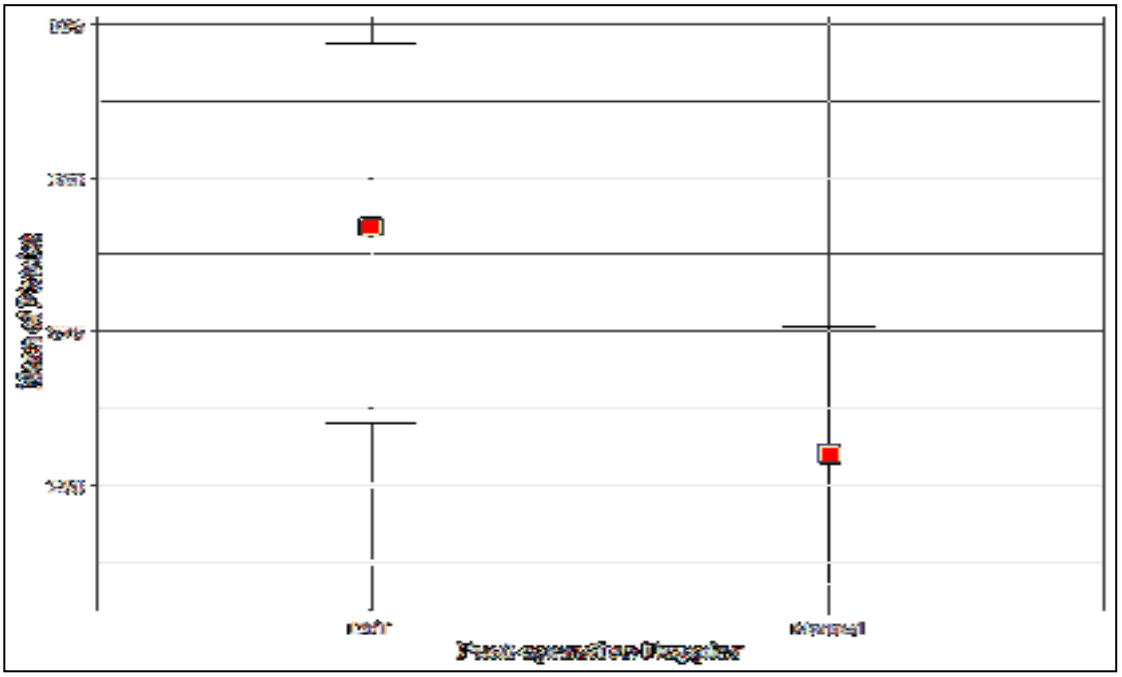


Figure 28: Mean of Platelet over post-operative Doppler study.

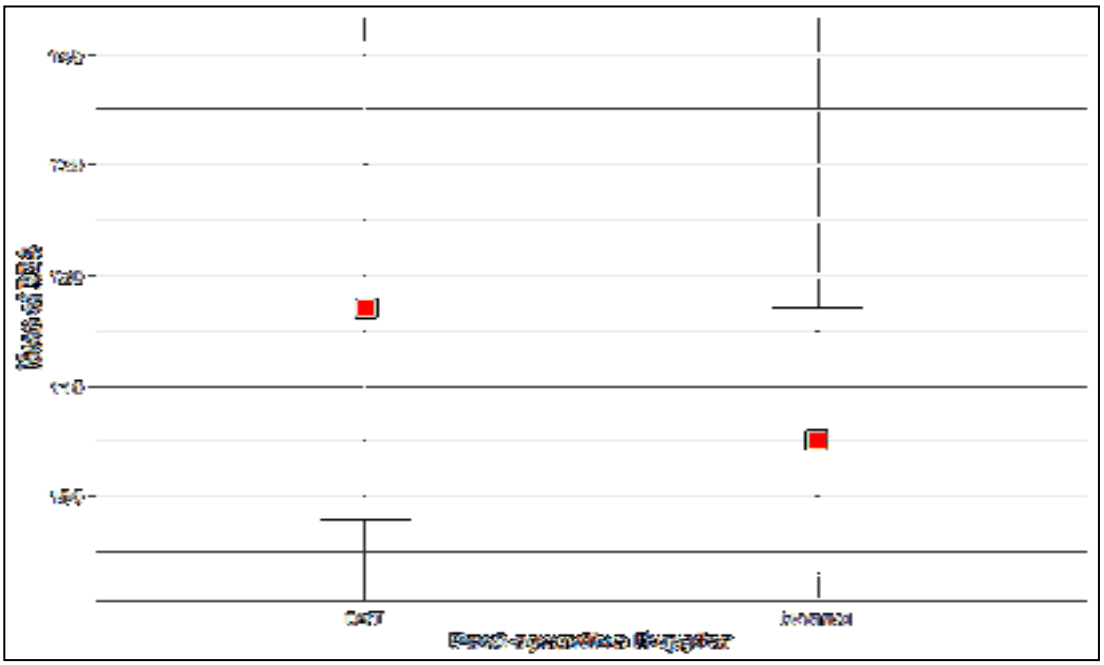


Figure 29: Mean of RBS over post-operative Doppler study.

		Number of subjects (%)
Post-operative DVT	Fractures around Hip joint	6 (66.67%)
	Fractures femur shaft	1 (11.11%)
	Fractures around Knee joint	1 (11.11%)
	Fractures of pelvis	1 (11.11%)
	Fractures Tibial Shaft	0 (0%)
	Fractures around Ankle joint	0 (0%)
Among Hip Fractures	Intertrochanteric fractures (IT)	3 (50.00%)
	Subtrochanteric fractures	1 (16.67%)
	Neck of femur fractures	2 (33.33%)

Below plots visualizes the above table.

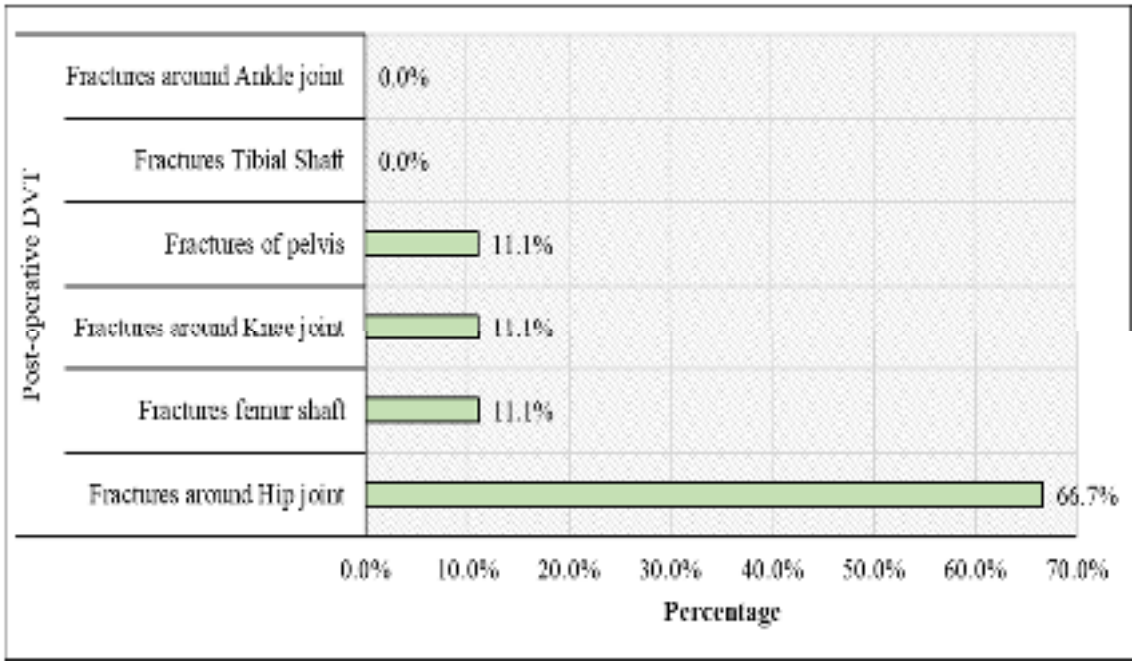


Figure 30: Distribution of subjects by post-operative DVT.

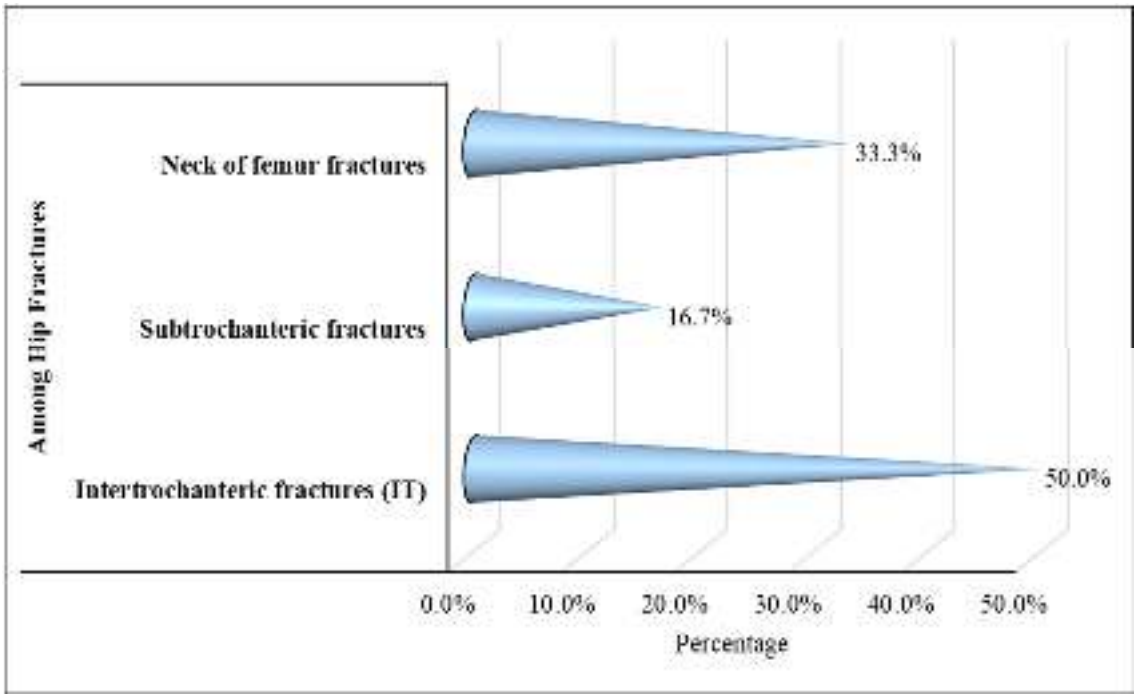


Figure 31: Distribution of subjects among hip fractures.

DISCUSSION

- DVT is medical condition characterized by formation of thrombus in veins of either lower or upper limb. Its risk factors comprise of smoking, alcohol intake, obesity, diabetes mellitus, connected tissue disorders, pregnancy, use of contraceptive pills, trauma, prolonged immobilization and surgeries.
- Devastating outcome related with this condition is PE. Patient developing PE will mostly have underlying symptoms of DVT. Though it is significant to note that patients with DVT do not always have symptoms, it is occasionally asymptomatic and can progress to deadly PE, thus it is critical to diagnose asymptomatic DVT patients as well.
- This observational research was completed in one year by studying 42 subjects who underwent major orthopaedic surgeries They were included in the study as per selection criteria. This research involved both sexes. This study comprised of 15 females and 27 males who were established to have diagnosis of lower limb fractures. Average age of subjects in research was 51.12±20.09 years. Similar research by Agarwala S et al.[69] reported an average age of about 65 years. Research conducted by Bhagwat A S[70] et al. reported the age in study was about 58 yrs. Research study conducted by Ashutosh P M et al.[71] reported the age in their study was nearly 60 years. Study by Jang MJ e. al. [72] et al average age in the study was about 60 years. All above studies showed that DVT is more commonly seen in ageing patients. This finding is in accordance with our research as similar finding was noted in our study.
- One of the well-recognized risk factor for thrombosis in venous system include orthopaedic surgeries due to various reasons like tissue thromboplastin release from associated soft tissues dissection and reaming of the bones. Prolonged

immobility due to surgeries leads to venous stasis. Virchow's triad explains pathogenesis of DVT after orthopaedic surgeries. All components of triad which involve endothelial injury, venous stasis and hypercoagulability are present after orthopaedic surgeries. Physiological changes after trauma promotes hypercoagulable state. Immobilization after orthopaedic surgeries and non-weight bearing of operative limb leads to venous stasis, thus explaining high DVT incidence after orthopaedic surgeries.

- In research conducted by Lim Y W et. al.[32] in which they included 104 patients with diagnosis of intertrochanteric fracture, sub-trochanteric fracture and neck femur fractures, colour - Doppler was performed on 5th day post-operatively. They concluded DVT incidence to be 8%. Various risk aspects determined were increasing age, habit of smoking, habit of alcohol intake, BMI >25, co morbid circumstances like diabetes mellitus. Their findings were similar with our results in relation to risk factors.
- Ya-Hui Fu et al.[28] conducted observational study for determination of DVT incidence following femur neck fractures. The subjects were evaluated with color Doppler prior and subsequent to operative procedure. After obtaining results of color doppler subject were categorised into thrombosis and non-thrombosis group. Doppler results revealed DVT incidence pre-operatively and post-operatively turned out to be 32% and 56% respectively**.** Blood loss, ORIF were risk aspects for DVT. This study showed higher DVT incidence in hip surgery cases, both pre and post –operatively, compared to our study.
- Thanainit C et al.[29] conducted study in which they included 97 subjects who had hip fractures. Bilateral contrast venography was performed as a diagnostic modality to diagnose DVT, incidence of DVT reported was 47%. Higher

incidence of DVT was seen in this study as compared to our study in which colour Doppler USG was used as a diagnostic modality.

- Dhillon K.S et al.[31] conducted similar prospective study in Malaysian population to evaluate DVT incidence after fracture hip. 88 patients were involved in research. High percentage of 62.5 % was noted. They reported very high incidence of DVT when compared to our study.
- Nagi O N et al.[73] reported the DVT incidence to be around 8% without thromobo-prophylaxis. Out of 50 patients studied, 4(8%) developed DVT post operatively. Color doppler was performed as a diagnostic modality. This study reported less incidence of DVT than our study.
- Ren Zhixin et. al.[42] conducted retrospective case control study to determine DVT incidence after femur shaft fractures. In study they included 308 patients with femur shaft fractures. Out of 308 patient 48 developed DVT. Risk factors associated with development of DVT were intraoperative blood loss, smoking, elderly age group. Reported incidence and risk aspects were consistent with our study.
- My Hanh Bui et al.[27] conducted a study in Vietnamese population by involving 92 subjects to determine DVT incidence after major orthopaedic surgeries. They performed color Doppler (pre and post operative) on fractured limb. DVT incidence in their study was 7%. Various risk aspects involved were old age, smoking and extended duration of immobilization. This study showed similar risk factors for development of DVT as seen in our study.
- Saket R et al[26] did a study in Indian population to determine incidence of DVT after proximal fractures of femur. 66 subjects were enrolled. DVT was present in 9 subjects among 66 subjects (13.6%). 5 patients out of 9 had clinical features.

The overall incidence of DVT in their study is less than our study.

- Park J S et al.[34] did study for lower limb DVT determination subsequent to fractures of hip joints. Out of total 901 patients, 337 received with thrombophylactic agents in accordance with guidelines established by their institute. Remaining patients did not obtain any prophylactic treatment. 2.7 % of patients developed thrombosis and 1.4% developed PE. They documented lower DVT incidence as compared to our study.
- Abelseth, G et al.[36] did a prospective study to evaluate DVT incidence in patient undergoing surgeries for lower limb distal to hip. 102 study participants were recruited for this research. All study subjects underwent surgeries for respective fractures. For all study participants bilateral venography was done. DVT incidence determined was 28 percent, highest after tibia plateau followed by femoral shaft and least in tibia plafond fracture. They documented high incidence which is consistent with our study.
- Ali Z et al.[38] conducted similar study and found DVT prevalence of 27% after hip and knee surgeries. The results of this study were similar to our study.
- Singh R et al.[37] did similar study and determined DVT incidence to be around 18.13 percent. Color doppler was performed after orthopaedic surgeries around hip and knee. The findings of our study are consistent with this study.
- There are various diagnostic modalities for DVT like contrast venography, colour Doppler study, Impedance plethysmography, MRV. Each diagnostic modality has its own advantages. Contrast venography is the gold standard for diagnosing DVT. It has certain limitations like invasive nature, usage of contrast agents which can cause anaphylaxis reaction and nephrotoxicity. Color doppler was used as a diagnostic modality in our study due to various reasons like it is non-invasive in

nature, no contrast is used and it has high sensitivity & specificity.

- In our study, incidence determined after major orthopaedic surgeries was 21.4%. Out of 9 DVT patients 5 were diagnosed with hip fractures. Risk factors were determined for DVT as secondary objectives. We found smoking, alcohol intake, DM, hypertension, BMI >25 were the self-determining risk aspects of DVT. Out of 9 DVT patients 7 had history of smoking, 6 had history of alcohol intake, 8 had BMI > 25, 7 had history diabetes mellitus.
- Gregory Piazza et. al.[74] conducted research to evaluate if diabetes is risk aspect for DVT. In his study total of 2468 thromboembolic subjects were evaluated and out of 2468, 476 patients had h/o diabetes hence it was concluded DM is the self-determining risk aspect for developing DVT. This finding is consistent with findings of our study.
- Yun-jiu cheng et al.[75] conducted research to evaluate if smoking is risk for DVT using literature search and determined that smoking aggravates the risk for development of DVT. They related DVT among smokers and non- smokers and concluded that risk for DVT is more among smokers. They also determined that risk for DVT increases with the increase in the quantity of cigarettes smoked. This is consistent with finding of our study as DVT was more among smokers in our study
- K.A.L.Darvall et al.[76], after gathering data from library database, did a study to evaluate if DVT & obesity are inter-linked with each other. They established obesity as a risk aspect for DVT which is consistent with findings of our study as out of 9 DVT positive patients 8 had BMI more than 30.

CONCLUSION

In this observational research, 42 subjects were included after approval of ethical committee and by following appropriate inclusion and exclusion criteria. After obtaining informed consent, all the study subjects were evaluated with pre-operative and post-operative Doppler ultrasonography for establishing DVT. Post-operative colour Doppler was performed on 5th post-operative day. Colour Doppler was performed as diagnostic modality because it offers many advantages like its non-invasive nature, has high sensitivity and specificity of 89 % and 100% respectively.

Out of 42 subjects there were 15 females and 27 males with mean age of 51.12±20.09. Among 42 subjects, 9 patients had established DVT after surgery. Incidence of DVT after major orthopaedic surgeries was determined to be 21.4%. All patients with DVT received treatment according to latest guidelines. Among 9 DVT patients 7 were smokers, 7 were diabetics, 8 had BMI >25, and 6 had history of alcohol intake thus suggesting that diabetes, alcohol intake, smoking and obesity were self-determining risk factors for DVT. Among fracture patterns, DVT was most common in fractures around hip. Out of 9 fracture patterns 3 patients had Intertrochanteric fracture, 2 patients had femur neck fractures, 1 had sub-trochanteric, 1 had patella fracture, 1 had acetabulum fracture and 1 had femur shaft fracture.

Results of our study and other previous studies show that DVT is more common in Indian population than it was thought and that DVT is most prevalent in patients with fractures around the hip, particularly in those having associated risk factors like smoking, diabetes and BMI >25. So, colour Doppler USG study should be used as a tool for screening DVT after major orthopaedic surgeries in such group of

patients, especially in elderly age group with associated risk factors and co-morbid conditions, so that its complications like PE, PTS can be prevented and mortality can be minimized after major orthopaedic surgeries.

SUMMARY

- This was hospital based observational study conducted over a period of 1 year.
- 42 patients were included in the study after selection process.
- Out of 42 patients 15 were females and 27 were males.
- Mean age in the study was 51.12±20.09 years.
- Pre-operative and post-operative color doppler was done to determine the incidence of lower limb DVT.
- Among 42 patients 9 were diagnosed to have DVT after major orthopaedic surgeries.
- Incidence of lower limb DVT determined after major orthopaedic surgeries was 21.4%.
- DVT was most prevalent in patients with hip fractures.
- Risk factors associated with DVT were obesity, smoking, alcohol intake and diabetes.

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ANNEXURE I
ETHICAL CLEARANCE.

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed to be University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/301 **Date: 24/12/2019**

To,

REGISTRATION NO. BL0119010
PG student in Orthopaedics,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"AN OBSERVATIONAL STUDY TO DETERMINE THE INCIDENCE OF LOWER LIMB DEEP VEIN THROMBOSIS AFTER MAJOR ORTHOPAEDICS SURGERIES"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE II: INFORMED CONSENT

Mr/Mrs-

You are invited to participate in this study

"AN OBSERVATIONAL STUDY TO DETERMINE THE INCIDENCE OF LOWER LIMB DEEP VEIN THROMBOSIS AFTER MAJOR ORTHOPAEDIC SURGERIES"

Principal investigator: **REGISTRATION NO. BL0119010.**

INTRODUCTION AND PURPOSE:

Deep Vein Thrombosis (DVT) is a common complication in case of lower limb trauma. It should be diagnosed and treated as early as possible to prevent complications like chronic pain, varicose veins, ulcers, by which the quality of life can be affected. Deep vein thrombosis can lead to fatal pulmonary embolism. It is estimated that 40-50% of untreated DVT patients will develop pulmonary embolism and about 9-10% will die in one hour. Thus, elucidating the incidence of deep vein thrombosis is a surrogate marker for pulmonary embolism which is of clinical importance.

OBJECTIVES:

Primary objectives

1. To determine incidence of lower limb DVT after major orthopaedic surgeries

Secondary objectives

2. To identify risk associations for DVT, such as diabetes, hypertension, smoking, and obesity.

PROCEDURE:

If you provide consent to be in this study, x rays will be done to diagnose

fracture pattern, relevant investigations will be done. Pre – operatively color doppler will be done. Post operatively color doppler will be done on post operative day 5. This doppler will be done after removal of slabs and dressings. This test will take around 20 mins.

If you decline to participate in study at any time your future health services will remain unchanged and you will receive standard treatment according to your illness

VOLUNTARY PARTICIPATION/ WITHDRAWL:

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part, I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The investigator or the sponsor may stop my participation in this study. I will tell of any important new findings that may change my willingness to continue to take part. If I choose not to take part in the study, I will receive the standard treatment for patients with my condition.

CONFIDENTIALITY:

All information collected about the you during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify the subject in this research record. Information from this study may be presented but your identity will be confidential in any publication.

If any enquiries in the future or in case of study related injury or illness, you may contact following person:

Principal investigator:

REGISTRATION NO. BL0119010

PG. Resident,

Department of orthopaedics,

JN Medical College,

Belagavi– 590010

Guide:

DR. _____

M.S.(ORTHO), MRCS(Ed), MCh(ortho)

Associate professor,

Department of orthopaedics,

JN Medical College,

Belagavi– 590010

Statement of consent

"I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and had all my questions answered. I will be given a copy of this consent form."

Signature of the Participant or legally authorized representative

Participant's Name: ……

Signature: ……

Name of legally authorized representative: ……..

Signature: …….

Witness's Name:

Signature: ……..

Investigators Name and Signature: …….

Date and Place: ……

ANNEXURE III : PROFORMA

Socio-demographic data

Name:		
Age:		
Gender:		
Occupation:		
Smoking status:	Yes ( )	No ( )
Drinking alcohol:	Yes ( )	No ( )

Clinical presentation:

Limb involved	Left low limb ( ) Right low limb ( )
Fracture type	Fractures around hip joint Fractures of pelvis Fracture femur shaft Fractures around knee joint Fractures of tibia shaft Fractures of ankle joint
Surgical type	CRIF with nailing ORIF with plating Hemiarthroplasty CRIF with external fixator ORIF with tension band wiring
History of deep venous thrombosis	Yes ( ) No ( )
If any history of anticoagulant intake	

Medical morbidity:

History of hypertension	Yes ( )	No ( )
History of any malignancy	Yes ( )	No ( )
History of Diabetes	Yes ( )	No ( )
History of Coronary heart disease	Yes ( )	No ( )
History of arrhythmia	Yes ( )	No ( )
History of Stroke		
Body Mass index (kg/m^2):		
Any other history of chronic illness		

Laboratory Investigations:

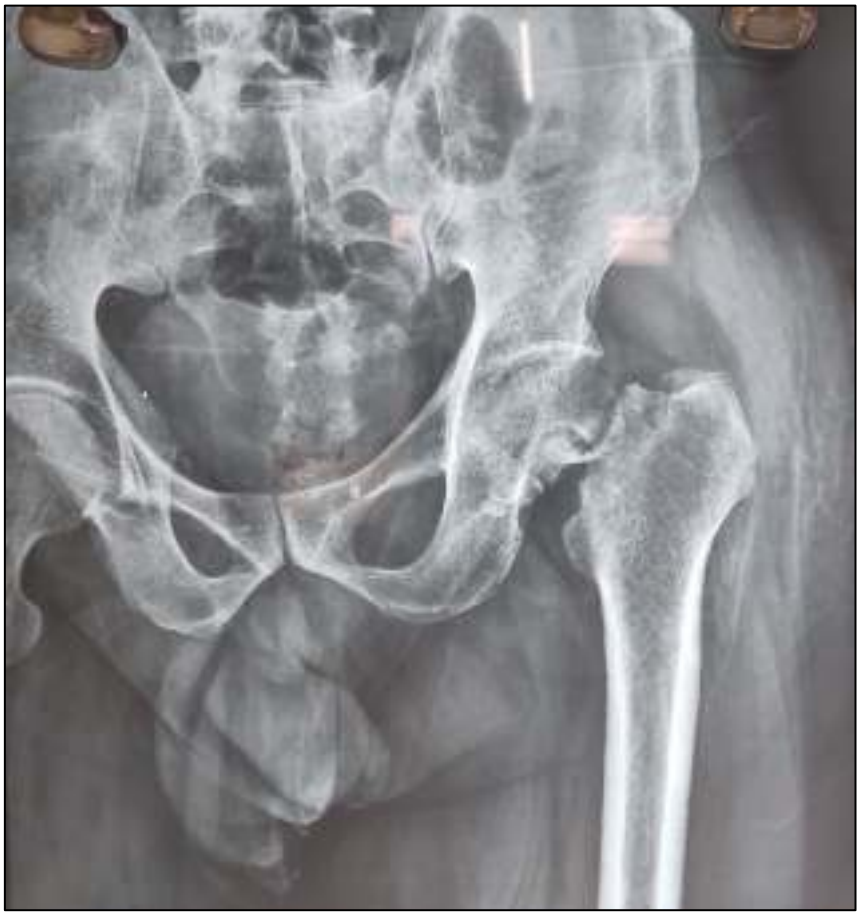
Haemoglobin levels	
Pre-operative color doppler evaluation	
Post-operative color doppler evaluation at Post-operative day 5	
D-dimer levels pre operatively	
D-dimer levels post operatively	
HsCRP levels pre operatively	
HsCRP levels post operatively	
Total cholesterol levels (mg/dL)	
Creatinine levels	
Platelet counts	
Required x rays	

Abbreviation- HsCRP Highly specific C reactive protein, BMI – Body mass index

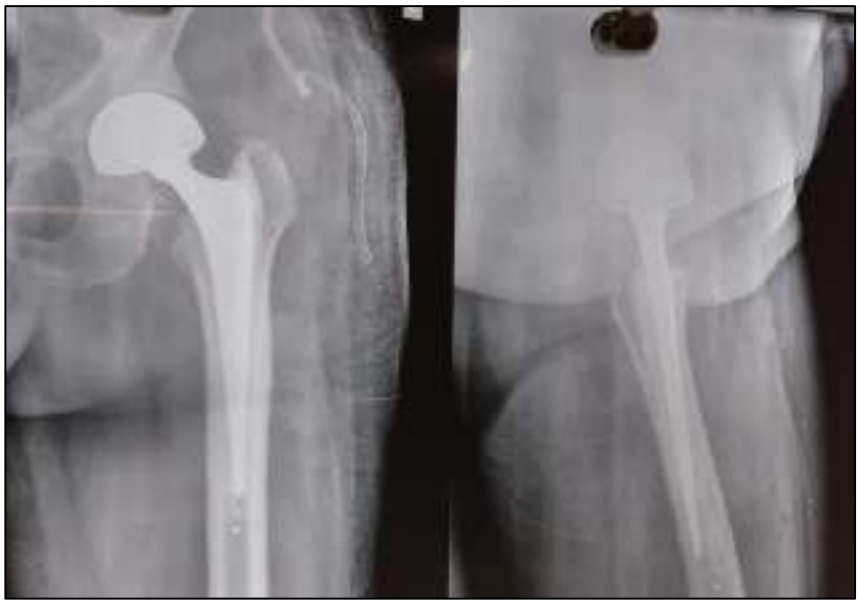
ANNEXURE IV

PHOTOGRAPHS

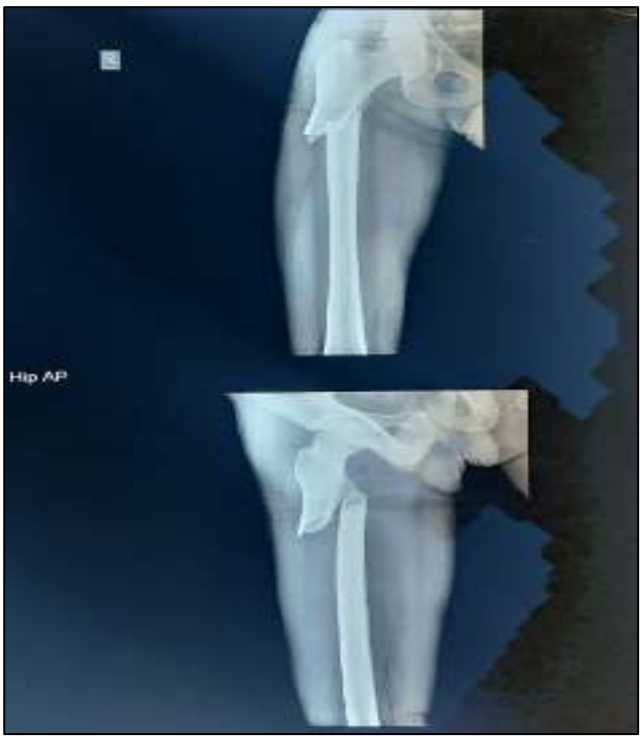
PHOTOGRAPH 1: DOPPLER USG APPRATUS



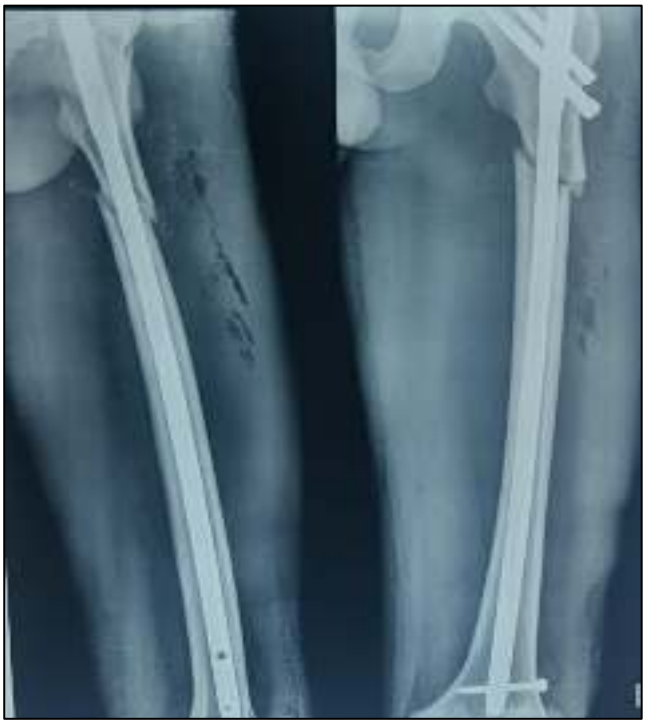
PHOTOGRAPH 2: PRE-OPERATIVE X RAY OF NECK OF FEMUR FRACTURE



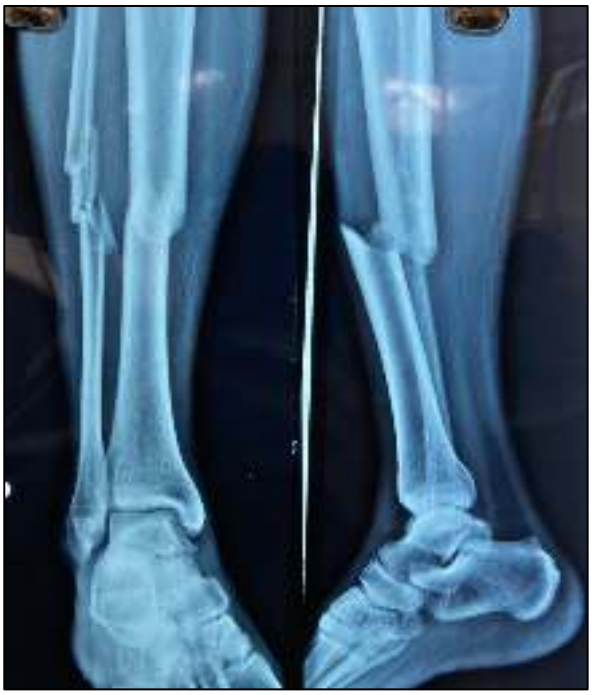
PHOTOGRAPH 3: HEMIARTHROPLASTY OF NECK OF FEMUR



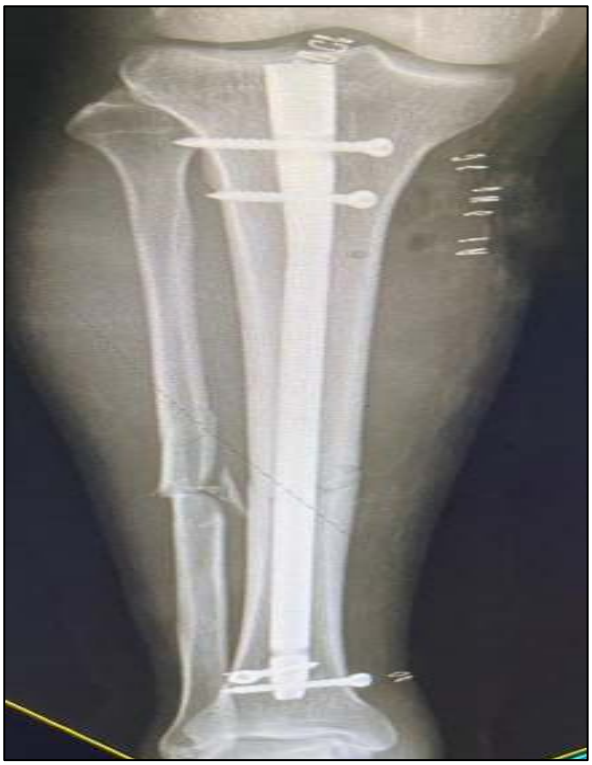
PHOTOGRAPH 4: PRE-OPERATIVE X RAY OF SUB-TROCHANTERIC FRACTURE



PHOTOGRAPH 5: POST-OPERATIVE X RAY OF SUB-TROCHANTERIC FRACTURE



PHOTOGRAPH 6: PRE OPERATIVE X RAY OF TIBIA AND FIBULA FRACTURE



PHOTOGRAPH 7: POST OPERATIVE X RAY OF TIBIA SHAFT FRACTURE

S. NO	AGE	SEX	DIAGNOSIS	TYPE OF OPERATION	PRE OPERATIVE DOPPLER EVALUATION	PRE OPERATIVE D DIMER LEVELS	PRE OPERATIVE HSCRP LEVELS	cholestrol levels	S CREATININE LEVELS	PLATLET COUNT	RBS	POST OPERATIVE DOPPLER EVALUATION	D DIMER LEVELS	HSCRP	SMOKING HISTORY	ALCOHAL INTAKE	BMI	DIABETES MELLITUS
1	28	MALE	RIGHT FEMUR SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	988 ng/ml	9.2	119 mg/dl	1.06	365	90 mg/dl	NORMAL DOPPLER STUDY	1337 ng/dl	48.4	ABSENT	ABSENT	<25	ABSENT
2	53	MALE	LEFT NECK OF FEMUR FRACTURE	HEMIARTHROPLASTY	SUPERFICIAL THROMBOPHLEBITIS	1120 ng/ml	67.9	106 mg/dl	1	247	112 mg/dl	NORMAL DOPPLER STUDY	1196 ng/dl	89.8	ABSENT	ABSENT	<25	ABSENT
3	75	MALE	RIGHT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	1160 ng/ml	11.9	89 mg/dl	1.48	141	153 mg/dl	NORMAL DOPPLER STUDY	1194 ng/dl	60	ABSENT	ABSENT	>25	ABSENT
4	74	FEMALE	LEFT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	781 ng/ml	11.3	141 mg/dl	1.2	287	90 mg/d;	NORMAL DOPPLER STUDY	1123ng/dl	62.1	ABSENT	ABSENT	>25	ABSENT
5	85	FEMALE	LEFT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	844 ng/ml	68.1	119 mg/dl	0.73	264	85 MG/DL	DEEP VEIN THROMBOSIS	1216 ng/dl	60.4	ABSENT	ABSENT	>25	PRESENT
6	62	MALE	SUPRACONDYLAR FEMUR FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	450 ng/dl	248.8	108 mg/dl	0.8	341	87 mg/dl	VARICOSE VEINS	1053 ng/dl	139.2	ABSENT	ABSENT	<25	ABSENT
7	68	MALE	LEFT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	1243 ng/DL	77.5	204 mg/dl	0.96	342	94 MG/DL	DEEP VEIN THROMBOSIS	1324 ng/dl	149.8	PRESENT	PRESENT	>25	PRESENT
8	55	FEMALE	LEFT FEMUR SHAFT FRACTURE	ORIF WITH MIPO	NORMAL DOPPLER STUDY	800ng/dl	89	140 mg/dl	0.56	349	90 mg/dl	DEEP VEIN THROMBOSIS	1224 ng/dl	89	ABSENT	ABSENT	>25	ABSENT
9	38	MALE	RIGHT TIBIA FRACTURE	CRIF WITH EX FIX	NORMAL DOPPLER STUDY	456ng/dl	34	127mg/dl	0.8	345	123 mg/dl	NORMAL DOPPLER STUDY	1222 ng/dl	98	ABSENT	ABSENT	<25	ABSENT
10	87	MALE	RIGHT NECK OF FEMUR FRACTURE	HEMIARTHROPLASTY	NORMAL DOPPLER STUDY	1123ng/dl	12.4	106 mg/dl	0.9	234	76 mg/dl	NORMAL DOPPLER STUDY	1234 ng/dl	123.3	ABSENT	ABSENT	<25	ABSENT
11	49	FEMALE	RIGHT TIBIA SHAFT FRACTURE	CRF WITH LRS	NORMAL DOPPLER STUDY	877 NG/DL	68	110 mg/dl	1.1	123	90 mg/dl	NORMAL DOPPLER STUDY	1234 ng/dl	123.5	ABSENT	ABSENT	<25	ABSENT
12	24	MALE	LEFT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	980 ng/ml	12	109 mg/dl	1	125	70mg/dl	NORMAL DOPPLER STUDY	1090ng/dl	129	ABSENT	ABSENT	<25	ABSENT
13	68	MALE	LEFT PATELA FRACRURE	TBW	NORMAL DOPPLER STUDY	970mg/dl	9.2	119mg/dl	1	365	95mg/dl	DEEP VEIN THROMBOSIS	1337ng/dl	48.4	PRESENT	PRESENT	>25	PRESENT
14	70	MALE	RIGHT ANKLE FRACTURE	ORIF WITH PLATING	NORMAL DOPPLER STUDY	400 ng/dl	60	110MG/DL	1.2	325	90MG/DL	NORMAL DOPPLER STUDY	100ng/dl	130	ABSENT	ABSENT	<25	ABSENT
15	29	MALE	RIGHT TIBIA FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUTY	700 ng/dl	11	200ng/dl	1.09	212	120mg/dl	NORMAL DOPPLER STUDY	1200ng/dl	120	ABSENT	ABSENT	<25	ABSENT
16	30	MALE	RIGHT NECK OF FEMUR FRACTURE	HEMIARTHROPLASTY	NORMAL DOPPLER STUDY	400ng/dl	12	112mg/dl	1.03	215	100mg/dl	DEEP VEIN THROMBOSIS	1100 ng/dl	120.5	PRESENT	PRESENT	>25	PRESENT
17	65	MALE	LEFT NECK OF FEMUR FRACTURE	HEMIARTHROPLASTY	NORMAL DOPPLER STUDY	200ng/dl	40	180mg/dl	1.2	340	160mg/dl	DEEP VEIN THROMBOSIS	900ng/dl	47.5	PRESENT	PRESENT	>25	PRESENT
18	61	MALE	RIGHT IT FRACTURE FEMUR	CRIF with PFN	NORMAL DOPPLER STUDY	530ng/dl	65	160mg/dl	1.07	329	120mg/dl	DEEP VEIN THROMBOSIS	766ng/dl	43.6	PRESENT	PRESENT	>25	PRESENT
19	21	FEMALE	LEFT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	121ng/dl	6.5	101MG/DL	0.76	300	90mg/dl	NORMAL DOPPLER STUDY	140ng/dl	8.9	ABSENT	ABSENT	<25	ABSENT
20	58	MALE	LEFT SUBTROCHANTERIC FRACTURE	CRIF WITH PFN	NORMAL DOPPLER STUDY	1370mg/dl	1.5	169mg/dl	0.52	260	100mg/dl	DEEP VEIN THROMBOSIS	1273ng/dl	119.5	PRESENT	PRESENT	>25	PRESENT
21	72	FEMALE	LEFT SUBTROCHANTERIC FRACTURE	CRIF WITH PFN	NORMAL DOPPLER STUDY	453ng/dl	11.2	93mg/dl	1.35	284	124mg/dl	NORMAL DOPPLER STUDY	1290ng/dl	29.4	ABSENT	ABSENT	<25	ABSENT
22	35	FEMALE	LEFT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	300ng/dl	12	120mg/dl	1	233	122mg/dl	NORMAL DOPPLER STUDY	1224ng/dl	43.5	ABSENT	ABSENT	<25	ABSENT
23	45	FEMALE	LEFT ACETABULAR FRACTURE	ORIF WITH PLATE	NORMAL DOPPLER STUDY	848ng/dl	350.4	157mg/dl	0.53	290	90mg/dl	DEEP VEIN THROMBOSIS	1200NG/DL	40.2	PRESENT	ABSENT	<25	ABSENT
24	21	MALE	LEFT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	961ng/dl	6.5	145mg/dl	0.87	219	90MG/DL	NORMAL DOPPLER STUDY	760NG/DL	18.8	PRESENT	ABSENT	<25	ABSENT
25	58	FEMALE	LEFT ANKLE FRACTURE	CRIF WITH EX FIX	NORMAL DOPPLER STUDY	342ng/dl	2.7	154mg/dl	0.64	285	199mg/dl	NORMAL DOPPLER STUDY	549 NG/DL	63.6	ABSENT	ABSENT	<25	ABSENT
26	60	FEMALE	RIGHT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	1001ng/dl	61.7	122mg/dl	0.9	144	90mg/dl	NORMAL DOPPLER STUDY	1499NG/DL	184	ABSENT	ABSENT	>25	ABSENT
27	28	MALE	RIGHT FEMUR SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	500ng/dl	54.7	129mg/dl	0.7	340	100mg/dl	NORMAL DOPPLER STUDY	1200ng/dl	148	PRESENT	ABSENT	>25	ABSENT
28	35	MALE	RIGHT SUBTROCHANTERIC FRACTURE	CRIF WITH PFN	NORMAL DOPPLER STUDY	450 ng/dl	45	129mg/dl	0.8	289	90MG/DL	NORMAL DOPPLER STUDY	1256ng/dl	67	PRESENT	ABSENT	>25	ABSENT
29	66	FEMALE	RIGHT NECK OF FEMUR FRACTURE	HEMIARTHROPLASTY	NORMAL DOPPLER STUDY	745ng/dl	34	123mg/dl	0.87	234	190mg/dl	NORMAL DOPPLER STUDY	1238ng/dl	90	ABSENT	ABSENT	<25	ABSENT
30	33	MALE	RIGHT TIBIA SHAFT FRACTURE	ORIF WITH PLATE	NORMAL DOPPLER STUDY	566ng/dl	45	120mg/dl	0.76	256	80mg/dl	NORMAL DOPPLER STUDY	500ng/dl	45	ABSENT	ABSENT	>25	ABSENT
31	24	MALE	RIGHT FEMUR SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	450 ng/dl	12	145mg/dl	0.9	284	100mg/dl	NORMAL DOPPLER STUDY	766ng/dl	184	ABSENT	ABSENT	<25	ABSENT
32	28	FEMALE	RIGHT FEMUR SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	1001ng/dl	34	154mg/dl	0.76	219	90mg/dl	NORMAL DOPPLER STUDY	140ng/dl	90	ABSENT	ABSENT	>25	ABSENT
33	65	FEMALE	RIGHT SUPRACONDYLAR FEMUR	CRIF WITH IMIL	NORMAL DOPPLER STUDY	400 ng/dl	61.7	120mg/dl	0.9	256	190mg/dl	NORMAL DOPPLER STUDY	766ng/dl	63.6	ABSENT	ABSENT	<25	ABSENT
34	23	MALE	LEFT FEMUR SHAFT FRACTURE	ORIF WITH IMIL	NORMAL DOPPLER STUDY	400 ng/dl	56	129mg/dl	1.09	245	100mg/dl	NORMAL DOPPLER STUDY	766ng/dl	45	ABSENT	PRESENT	>25	ABSENT
35	28	MALE	SUPRACONDYLAR FEMUR FRACTURE	ORIF WITH PLATING	NORMAL DOPPLER STUDY	745ng/dl	23.3	120mg/dl	0.7	234	90MG/DL	NORMAL DOPPLER STUDY	1337 ng/dl	63.6	ABSENT	PRESENT	<25	ABSENT
36	65	MALE	LEFT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	121ng/dl	65.4	134mg/dl	0.8	235	95mg/dl	NORMAL DOPPLER STUDY	1256ng/dl	90	ABSENT	PRESENT	>25	ABSENT
37	53	FEMALE	LEFT IT FRACTURE FEMUR	CRIF WITH PFN	NORMAL DOPPLER STUDY	961ng/dl	34.3	154mg/dl	0.7	236	100mg/dl	NORMAL DOPPLER STUDY	500ng/dl	8.9	ABSENT	ABSENT	<25	ABSENT
38	54	MALE	RIGHT IT FRACTURE FEMUR	CRIF WITH DHS	NORMAL DOPPLER STUDY	450 ng/dl	45.6	129mg/dl	0.78	258	100mg/dl	NORMAL DOPPLER STUDY	1337 ng/dl	123.3	ABSENT	ABSENT	>25	ABSENT
39	29	MALE	RIGHT TIBIA SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	745ng/dl	21.4	154mg/dl	0.9	246	122mg/dl	NORMAL DOPPLER STUDY	766ng/dl	89	ABSENT	ABSENT	<25	ABSENT
40	61	Male	RIGHT IT FRACTURE FEMUR	CRIF WITH IMIL	NORMAL DOPPLER STUDY	566ng/dl	45.6	101MG/DL	0.67	246	90MG/DL	NORMAL DOPPLER STUDY	500ng/dl	43.6	ABSENT	ABSENT	<25	ABSENT
41	65	FEMALE	RIGHT SUBTROCHANTERIC FRACTURE	CRIF WITH PFN	NORMAL DOPPLER STUDY	453ng/dl	23.9	129mg/dl	0.8	257	190mg/dl	NORMAL DOPPLER STUDY	1324 ng/dl	29.4	ABSENT	ABSENT	<25	PRESENT
42	34	MALE	LEFT FEMUR SHAFT FRACTURE	CRIF WITH IMIL	NORMAL DOPPLER STUDY	121ng/dl	2.5	93mg/dl	0.78	256	120mg/dl	NORMAL DOPPLER STUDY	1256ng/dl	48.4	PRESENT	ABSENT	<25	PRESENT