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A comparative study of colour doppler findings in diabetic and non-diabetic lower limb deep vein thrombosis patients attending tertiary care hospital

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Abstract
Introduction: Diabetes mellitus (DM) has been shown to be associated with increased coagulability, endothelial damage, and decreased fibrinolysis function [1], which can result in deep vein thrombosis (DVT). The present study was aimed at comparing the clinical characteristics of DVT patients with and without DM.
Methodology: We included 100 diabetic and 100 non-diabetic controls, who were was admitted in the indoor ward of medical and surgical departments and were referred to our department with suspicion of DVT. They underwent examination for DVT detection using ultrasonography machine on B-mode and colour Doppler study.
Results: Of the 100 diabetics and 100 non-diabetics, 21% and 15% had DVT respectively. Most of the thrombi were chronic, complete, proximal and single left sided. Common iliac vein (n = 10/21 vs 2/15; p value <0.05), External iliac vein (n=8/21vs 01/15; p value <0.05), Common femoral vein (n=17/21 vs 06/15 ; p value <0.05), Femoral vein (15/21 vs 05/15) and popliteal vein (n = 18/21 vs 9/15; p value <0.05) were found to be significantly more common among diabetics as compared to non-diabetics. Proportion of patients with involvement Posterior tibial vein, Anterior tibial vein and Peroneal vein were similar between DM and non-DM patients in our study. When assessed for complications from DVT, pain was found to be significantly more common among patients with DM as compared to non-DM, while complaints of edema were similarly distributed among the two patient groups.
Conclusions: Incidence of deep vein thrombosis in diabetic and non-diabetic patients differs, however it is not statistically significant. Accurate anatomic description of thrombus with the help of ultrasonography can help the clinician evaluate the course of thrombosis and optimize treatment.

Keywords: deep venous thrombosis, diabetes mellitus, duplex scanning, venous thromboembolism

Introduction
Venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) can be life threatening. Many factors have been studied to increase the incidence of DVT, including increasing age, obesity, congestive heart failure, a history of DVT/PE, cancer, and immobilization. Virchow proposed venous stasis, increased coagulability of the blood, and damage to the vessel wall as three precipitants for venous thrombosis. Diabetes mellitus (DM) has reached pandemic proportions across the globe and the burden is specially high in India. DM has been proven to be associated with increased coagulability, endothelial damage, and decreased fibrinolysis function [1], It is known that diabetes can contribute to the increase in cardiovascular events [2], which is confined to the arterial system, and also result in an increased risk of venous thromboembolism. The proposed mechanisms to explain this hypercoagulable state in hyperglycemia may be the loss of the endothelial glycocalyx layer harboring the coagulation factors, the glycation of coagulation factors altering their activity, or an effect on the transcription of their genes. Hyperinsulinemia, which is often present in type 2 diabetes has been shown to have a prothrombotic effect as well. A meta-analysis reported a 1.4-fold increase in the VTE risk for patients with diabetes (OR, 1.42; 95% CI, 1.12 to 1.77) [3]. There is limited studies which have assessed the effect of diabetes on DVT in Indian patients. The present study was aimed at comparing the clinical characteristics of DVT patients with and without DM

Methodology

Study design and sampling

The present observational study was conducted in the Department of Radiodiagnosis of a tertiary level care teaching hospital over a period of one year. We included 100 diabetic patients and 100 non-diabetic controls, who were was admitted in the indoor ward of medical and surgical departments and were referred to our department with suspicion of DVT. We excluded patients aged less than 18 years of age, with history of known coagulation disorders, or those who refused consent. All of these patients were explained the purpose of the study and an informed written consent was obtained before they were enrolled for the study. The study was approved by the Institutional Ethics Committee.

Data collection and data analysis

Patients underwent examination for DVT detection using ultrasonography machine on B-mode and colour Doppler study. The patients were examined in a sitting or in reverse Trendelenburg's position at about 10 to 15 degrees. The assessment included examination of the bilateral Common iliac vein, External iliac vein, common femoral vein, femoral vein, popliteal vein, anterior tibial vein and posterior tibial vein and peroneal vein. A diagnosis of DVT was made in the case of visualization of thrombus, absence of flow, lack of compressibility, or lack of augmentation. Compression technique was used to assess complete/partial thrombosis, Valsalva maneuver to assess proximal obstruction and augmentation to evaluate patency of distal veins. Iliac veins were examined in those patients who either had abnormal Doppler signals or had findings suggestive of obstruction at the level of groin. Using a pre-designed semi-structured study proforma, demographic information of the patients like age and gender was noted. History of the presenting complaints was obtained to assess the duration of thrombus. The extent, location, limbs and specific veins involved were noted. Patients were examined for the presence of complications like pain and edema.

The data were analysed in SPSS (version 23, IBM). Data were described as means and standard deviation for

Results

During the study period, we included a total of 200 hospitalized patients, half of which were diabetics. Of the 100 diabetics, 21 (21%) had DVT and among the rest of the 100 non-diabetics 15 (15%) had DVT. The difference in the incidence of DVT among diabetics and non-diabetics was not statistically significant (p value = 0.27). Table 1 describes the baseline characteristics of the patients included in the study. Mean age of the patients was 52.3 and 54.3 years in DM and non-DM groups respectively, the most common age group was 50 to 70 years of age in both the groups and both the groups had predominantly male patients. Most of the thrombus were chronic (n=10 in DM and n=8 in non-DM). Complete thrombus were found in majority of the patients (n=14 in DM and n=11 in non-DM). Both the study groups had patients with proximal thrombi and single left sided thrombi more commonly. Diabetics had 18 proximal and 11 distal thrombi, while non-diabetics had 11 proximal and 8 distal thrombi. Both the study groups were statistically similar with respect to their baseline characteristics. Table 2 describes and compares the distribution of patients with respect to the veins involved. Common iliac vein (n = 10/21 vs 2/15; p value <0.05), external iliac (n=8/21 vs 1/15, p value <0.05), common femoral vein (n = 17/21 vs 6/15; p value <0.05), femoral vein (n = 15/21 vs 5/15; p value <0.05) and popliteal vein (n = 18/21 vs 9/15; p value <0.05) were found to be significantly more common among diabetics as compared to non-diabetics. Proportion of patients with involvement of posterior tibial, anterior tibial and peroneal vein were similar between DM and non-DM patients in our study. When assessed for complications from DVT, pain was found to be significantly less common among patients with DM as compared to non-DM, while complaints of edema were similarly distributed among the two patient groups.

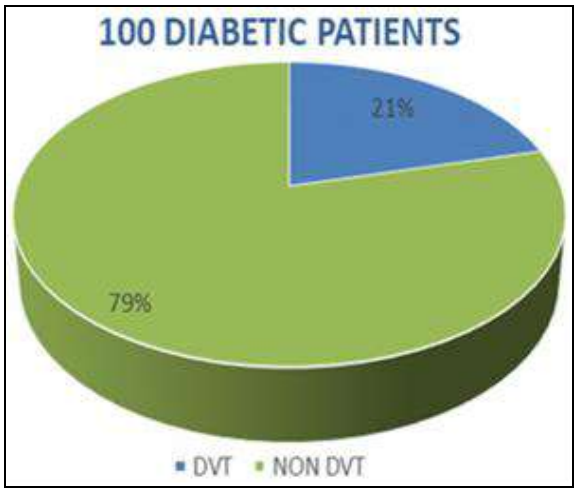

Fig 1: Percentage of DVT in diabetic patients

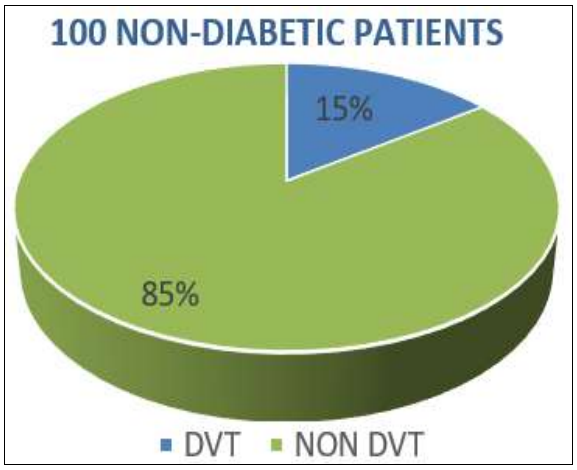

Fig 2: Percentage of DVT in non-diabetic patients

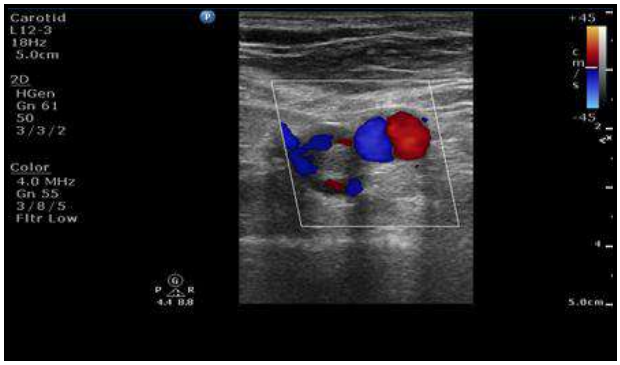

Fig 3: Color mode image showing partial, chronic thrombosis of common femoral vein.

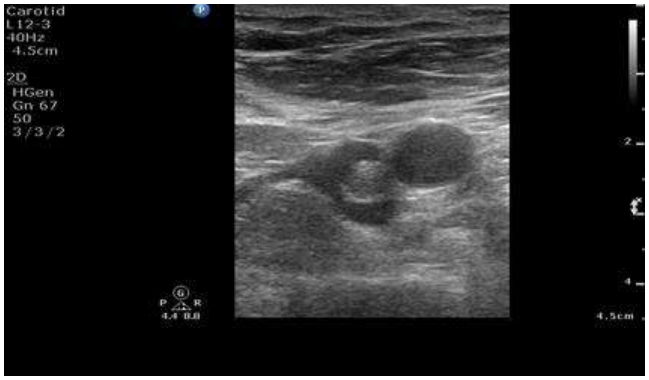

Fig 4: Transverse B-mode image showing partial, chronic thrombosis of common femoral vein in a diabetic patient.

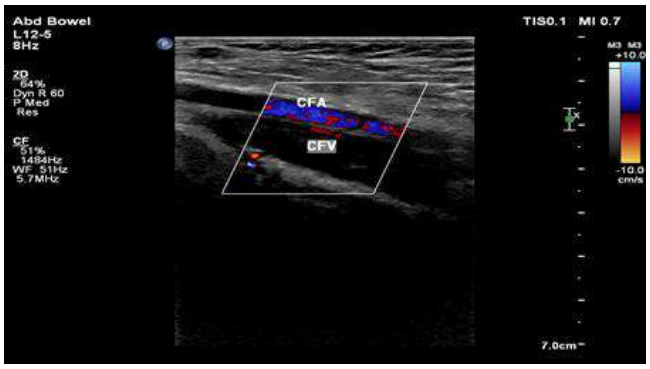

Fig 5: Longitudinal color mode image showing completely occluding anechoic thrombus in common femoral vein suggests acute complete thrombosis in a diabetic patient

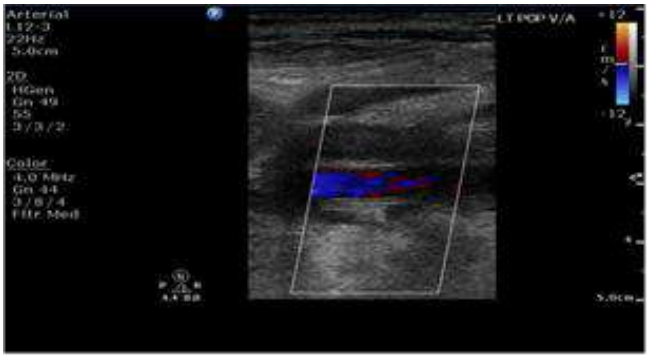

Fig 6: Longitudinal color mode image showing no flow in popliteal vein and mildly echogenic lumen causing slightly increase in diameter of vein as compare to accompanying artery suggests subacute complete thrombosis in a diabetic patient

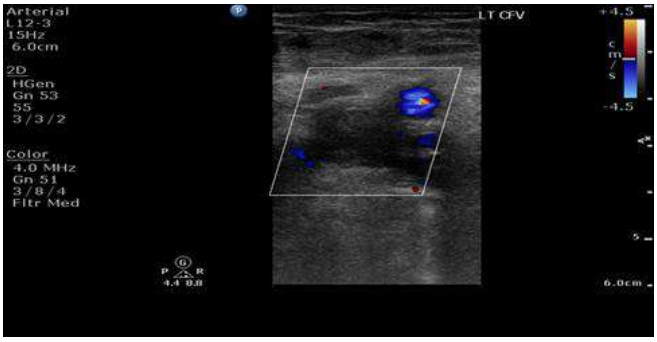

Fig 7: Transverse color mode image showing complete thrombosis of common femoral vein, accompanying common femoral artery shows normal flow in a diabetic patient.

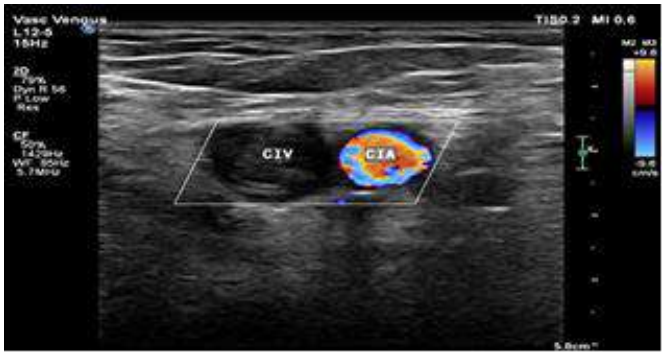

Fig 8: Transverse Color mode image showing complete thrombosis of common iliac vein in a diabetic patient.

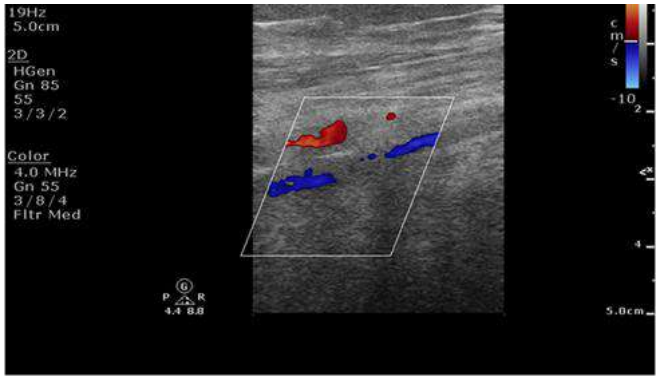

Fig 9: Longitudinal color mode image showing partial absent flow in lumen of posterior tibial vein suggestive of partial occluding thrombus in a non – diabetic patient

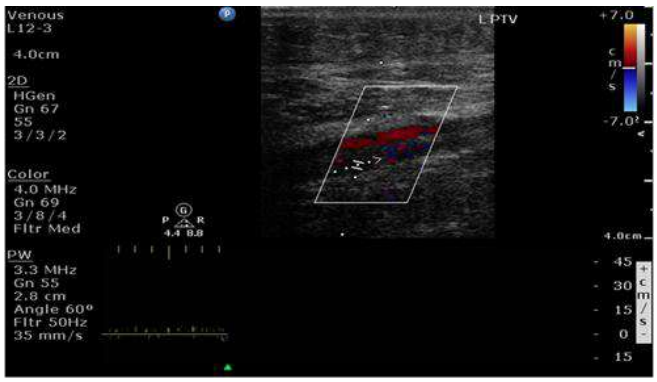

Fig 10: Longitudinal color mode image showing partial absent flow in lumen of posterior tibial vein suggestive of partial occluding thrombus in a non – diabetic patient.

Discussion

The present study compared the clinical spectrum of DVT patients with and without diabetes. The incidence of DVT was found to be 21% among diabetics and 15% among non-diabetic hospitalized. The two groups were similar with respect to stage, extend and location of thrombus. Previous studies have demonstrated a 1.4 fold increase in the VTE risk in patients with diabetes [**Error! Bookmark not defined.**]. Although the association between diabetes and VTE was robust, the causative nature of this association remains undetermined, as majority of the studies are of observational design. As a result, causality, inverse causality and confounding must be kept in mind while interpreting the results of these studies. A recent meta-analysis found that the association of VTE and DM was no longer significant when adjusted for co-morbid conditions [4]. Therefore, the observed association between diabetes and VTE appears to

be mainly explained by diabetes-associated comorbid conditions. We found that the most common age group among DVT patients was 50 to 70 years of age and had predominantly male patients. Khaladkar *et al*. found similar demographic characteristics in their 78 patients with DVT [5]. Furthermore, higher incidence among males could be due to significantly high levels of homocysteine (thrombophilia marker) in males as compared to females as reported in an Indian study [6].

Anatomic localization of the thrombus revealed that common iliac, external iliac, common femoral, femoral and popliteal vein involvement was more common among diabetics as compared to non-diabetics. Furthermore, DVT of the popliteal vein was the most common among all patients and left lower limb was most commonly involved in our patients, which was has been demonstrated in previous studies as well. Naqvi *et al*. also found that left limb was more frequently involved (65.87% vs. 27.30%) in their population [7], which was observed in our study as well. Patients with anatomical compression of the left common iliac vein by the left common iliac artery are prone to develop venous flow stasis in the left limb. This is also the reason for high prevalence of left limb DVT in pregnancy. We also found proximal thrombus to be more common as compared to distal ones. Previous studies have suggested that 60% of the DVT among Asians are proximal [8]. Pain was found to be less common among DM patients in our study as compared to non-DM, while edema was seen similarly among all patients. Similar results were reported by Piazza *et al*. who found that there was lower extremity pain in diabetic patients as compared to non-diabetic patients [9].

We diagnosed DVT using colour Doppler. Venography and pulmonary angiography are the gold standard for diagnosis of DVT and PE respectively [10]. Perhaps the relatively high cost of these tests and limited availability of such procedures result in lower utilization in India and Doppler ultrasonography still remains the widespread diagnostic modality for detecting DVT in India. In addition, duplex ultrasonography has a sensitivity and specificity of about 95% and 98%, respectively, for detecting DVT in symptomatic patients [**Error! Bookmark not defined.**].

There are a few limitations in our study. First, although Doppler ultrasonography is a non- invasive procedure and provides good accuracy for detecting DVT, the gold standard for detecting DVT is bilateral venography, which was not used in the present study. Second, the diagnosis of DVT can be affected by the level of expertise and years of experience of the sonographer. Therefore, the results of the present might not be applicable to other imaging centres. Second, data on numerous factors which might affect the incidence and severity of DVT like BMI, serum triglycerides and co-morbidites were not collected and analysed. Last, we did not analyse type-1 diabetes and type-2 diabetes separately due to small sample size, although they can have different influences on venous thrombosis.

Table 1: Baseline characteristics of the patients included in the study

Variables	Diabetes mellitus (n=21)	Non-diabetes mellitus (n=15)	p value
Age group (in years)			
≤ 30	1	0	
>30 to 50	6	6	0.88
> 50 to 70	11	5	
> 70	3	4	
Gender			
Females	6	4	0.99
Males	15	11	
Stage of thrombus			
Acute	6	4	
Subacute	5	3	0.89
Chronic	10	8	
Extend of thrombus			
Partial	7	4	0.75
Complete	14	11	
Location of thrombus			
Proximal	10	7	
Distal	3	4	0.94
Both (prox + distal)	8	4	
Limbs involved			
Single right	5	5	
Single left	15	9	0.18
Bilateral	1	1	

Table 2: Distribution of patients according to the veins involved

Veins	Diabetes mellitus (n=21)	Non-diabetes mellitus (n=15)	p value
Common iliac	10	02	<0.05
External iliac	08	01	<0.05
Common femoral vein	17	06	<0.05
Femoral vein	15	05	<0.05
Popliteal vein	18	09	<0.05
Posterior tibial vein	11	08	0.76
Anterior tibial vein	08	07	0.52
Peroneal vein	04	02	0.41

Table 3: Distribution of patients according to their complications

Complications	Diabetes mellitus (n=21)	Non-diabetes mellitus (n=15)	p value
Pain	5	12	<0.05
Edema	8	9	0.22

Conclusion

Incidence of deep vein thrombosis in diabetic and non-diabetic patients differs, however it is not statistically significant.

Anatomic localization of the thrombus revealed that common iliac vein, common femoral, femoral vein and popliteal vein involvement was more common among diabetics as compared to non-diabetics.

Distal veins like anterior tibial vein, posterior tibial vein and peroneal veins shows were almost similar in DM and non-DM patients.

There is no significant mean age difference between diabetic and non- diabetic in onset of DVT.

Symptoms like pain were significant more in non- diabetic as compared to diabetic.

Doppler ultrasonography serve as reliable, non-invasive and rapid investigation to detect DVT. Therefore helping in early detection of DVT in clinically suspected patients and in prevention of morbidity and mortality among hospitalized patients. Accurate anatomic description of thrombus which includes extend and location of the thrombus can help the clinician evaluate the course of thrombosis and optimize treatment.

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