Study of central venous catheter associated thrombosis in critically ill patients

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ABSTRACT

Venous thromboembolism (VTE) remains a major cause of morbidity and mortality. There are three factors that contribute to DVT.These factors are called Virchow's triad :venous stasis,hypercoagulability and changes in the endothelial blood vessel lining . Upper extremity deep vein thrombosis (UEDVT) is an increasingly recognized complication in medical ICU, especially after the increase in usage of central venous catheters (CVC) for different purposes.In our study we aimed to determine the prevelance and risk factors that make the incidence of central line associated deep venous thrombosis increase.

This descriptive study was conducted on 80 critically ill patients with inserted central venous catheter.

Venous duplex was done before, 5th and 10th day of (CVC) insertion.

KEY WORDS:Central venous catheter, pulmonary embolism, upper extremity deep vein thrombosis, venous duplex.

INTRODUCTION

Central venous catheters (CVCs) have an essential part in the management of critically ill patients .They are useful for hemodynamic monitoring as well as for administration of specific medications like vasopressors, parenteral nutrition and hemodialysis. These are associated with substantial risk of complications which can be mechanical, septic and thrombotic**.**

Deep vein thrombosis and pulmonary embolism are evolving and becoming well known to the public. They are both conditions that are recognized to have life-threatening consequences. The focus for deep vein thrombosis and pulmonary embolism has been mostly on the lower extremities. Upper extremity thrombosis is normally viewed as a more benign entity, but recent data suggested that the significance of morbidity and mortality is equal to that of the lower extremities. The prevalence of upper extremity thrombosis has increased due to the increase in usage of central venous catheters.Although, a majority of patients present with pain, swelling or prominent veins throughout the upper extremity, many patients will present as asymptomatic.

PATIENTS AND METHODS

The aim of this work is to study the prevelance of central venous catheter associated venous thrombosis in ICU patients using venous Doppler. All patients were subjected to:

1-Full history

It included age, sex, HTN, DM, malignancy, autoimmune diseases, cause of admission and type of CVC.

2-Clinical examination

3-Laboratory survey (CBC, kidney function tests, liver enzymes, D-dimer, Lipid profile)

4-Radiological imaging as indicated.

5- Venous duplex:

All patients were subjected to venous duplex of IJV and SCV at the site of catheter to determine if there is a deep venous thrombosis associated to CVC or not.

RESULTS

- Character of the thrombus: hypoechoic, homogenous and adherent to the wall of the internal jugular vein.
- Diameter: transverse diameter which was encroaching the lumen ranged from 5 to 11 mm and longitudinal diameter which was adherent to the vessel ranged from 16 to 32 mm. Lumen obstruction ranged from 25% to 55%. (Figure 9)

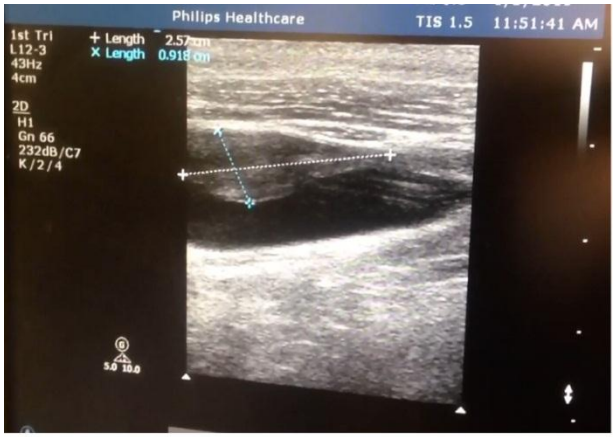


Figure (9)

- **Comparisons of demographic characters in different thrombotic outcomes:**

There was no statistically significant difference between study groups regarding age and sex. (Table 8)

Table (8): Comparisons of demographic characters in different thrombotic outcomes.

Variables	**No thrombosis** (number=62)		**Thrombosis** (number=18)		**p-value**	**Sig.**
Age (years)						
Mean /SD	57.8±19.1		56.8±16.9		0.9	NS
Sex						
Male	34	55%	10	55.6%	0.8	NS
Female	28	45%	8	44.4%		

Sig:significance,SD:standard deviation,NS:not significant.

- **Comparisons of risk factors in different thrombotic outcomes:**

There was statistically significant difference between groups regarding presence of autoimmune disease, and malignancy with higher percentage of thrombosis among patients with autoimmune disease (5 cases) (27.8%), and malignancy (7 cases) (38.9%).Autoimmune diseases carried significant high risk of thrombosis (Risk Ratio: 7.5) and malignancy carried risk ratio 7.25 for catheter related thrombosis.

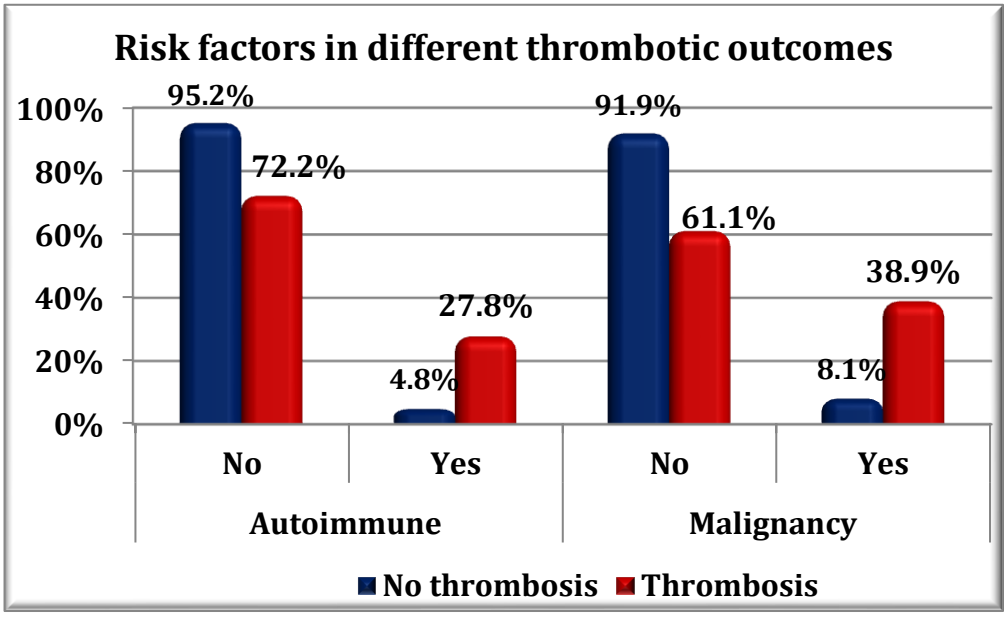
On the other hand there was no statistically significant difference regarding presence of hypertension and diabetes mellitus. (Table 9, Figure 10).

Table (9): Comparisons of risk factors in different thrombotic outcomes.

Variables	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.	Risk Ratio
	No.	%	No.	%			
HTN							
No	35	56.5%	12	66.7%	0.6	NS	-----
Yes	27	43.5%	6	33.3%			
DM							
No	41	66.1%	15	83.3%	0.2	NS	-----
Yes	21	33.9%	3	16.7%			
Autoimmune							
No	59	95.2%	13	72.2%	**0.01**	**S**	**7.5**
Yes	3	4.8%	5	27.8%			
Malignancy							
No	57	91.9%	11	61.1%	**0.004**	**HS**	**7.25**
Yes	5	8.1%	7	38.9%			

sig:significance,HTN:hypertension,DM:diabetes mellitus,

NS:notsignificant,S:significant,HS:highly significant.



Figure(10)

- **Comparison of types of malignancy in different thrombotic outcomes:**

Regarding specific types of malignancy, bladder cancer was associated with the most

significant high risk of catheter related thrombosis (risk ratio is very high and can't be calculated).It also may be due to the usage of large caliber dialysis catheters i.e. Mahurkars.There was statistically significant difference between study groups with higher percentage of thrombosis (16.7%).

Other malignancies i.e. bronchogenic carcinoma, lymphoma and patients associated with brain metastasis also carried high risk (risk ratio: 3.7, 3.64, 3.64 respectively) although this risk was not statistically significant. (Table 10)

Table (10): Comparison of types of malignancy in different thrombotic outcomes.

Variables	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.	Risk Ratio
	No.	%	No.	%			
Bladder cancer	0	0%	**3**	**16.7%**	**0.01**	**S**	*
Breast cancer	2	3.2%	1	5.6%	0.5	NS	1.76
Hepatocellular carcinoma	1	1.6%	0	0%	0.8	NS	0
Bronchogenic carcinoma	2	3.2%	2	11.1%	0.2	NS	3.75
Lymphoma	0	0%	1	5.6%	0.2	NS	*
Brain Metastasis	1	1.6%	1	5.6%	0.4	NS	3.64

***: very high risk ratio and can't be statistically calculated, S: significant, NS: not significant.**

- **Study of the effect of co morbidities on thrombotic outcomes:**

There was statistically significant difference between study groups regarding presence of chronic kidney disease with higher percentage of thrombosis (27.8%) among patients with CKD and shocked patients on vasopressors.

On the other hand there was no statistically significant difference regarding presence of other comorbidities.(Table 11).

Table (11): Comparisons of co morbidities in different thrombotic outcomes.

Variables	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.
	No.	%	No.	%		
SLE	3	4.8%	3	16.7%	0.1	NS
AKI	10	16.1%	4	22.2%	0.5	NS
CKD	1	1.6%	**5**	**27.8%**	**0.002**	**HS**
Shocked	15	24.2%	10	55.6%	0.02	S
Respiratory failure I	12	19.4%	5	27.8%	0.3	NS
Respiratory failure II	11	17.7%	1	5.6%	0.3	NS
Stroke	9	14.5%	2	11.1%	0.9	NS
Hepatic encephalopathy	2	3.2%	0	0%	0.9	NS
Diabetic ketoacidosis	4	6.5%	0	0%	0.6	NS

Primary Anti-phospholipid syndrome	0	0%	1	5.6%	0.2	NS
Rheumatoid arthritis	1	1.6%	0	0%	0.9	NS

n:number,sig:significance,AKI:acute kidney injury,SLE:systemic lupus erythematosus, CKD:chronic kidney disease,NS:not significant,HS:highly significant,S:significant.

- **Study of using vasopressors on different thrombotic outcomes:**

There was statistically significant difference between study groups regarding using vasopressor with higher percentage of thrombosis (55.6%) among patients who used vasopressor.(Table 12,Figure 11).

Table (12): Comparisons of using vasopressor in different thrombotic outcomes.

Vasopressor	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.
	No.	%	No.	%		
No	47	75.8%	8	44.4%	0.02	S
Yes	15	24.2%	10	55.6%		

Sig: significance, S: significant.

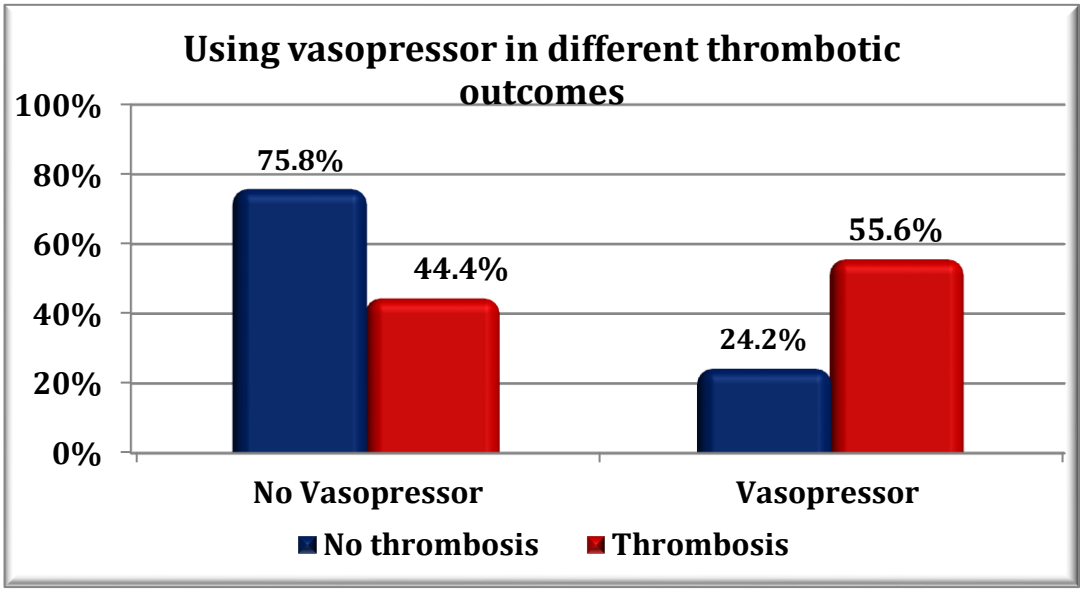


Figure (11)

- **Comparisons of Central line types in different thrombotic outcomes:**

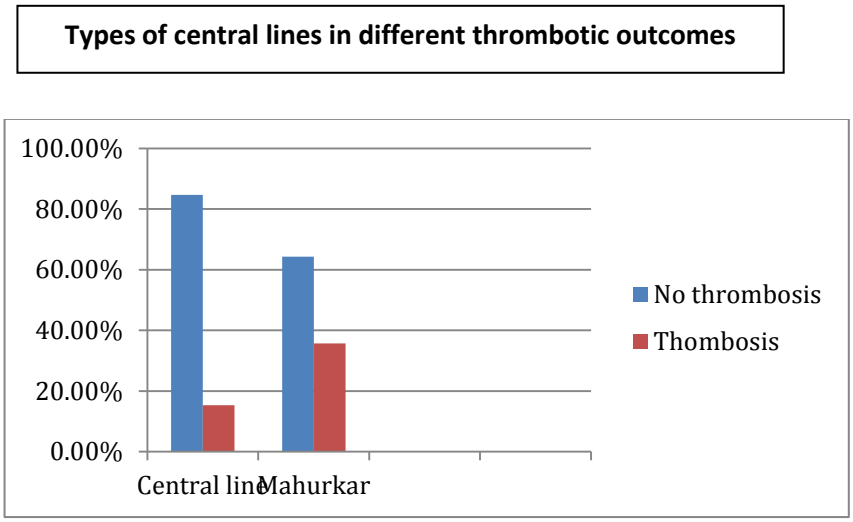
There was statistically significant difference between study groups regarding types of central line with higher percentage of thrombosis among patients who used Mahukar type(35.7%) compared to patients who used central venous line catheter(15.3%) with p-value 0.05.

The calculated risk ratio for occurrence of catheter related thrombosis revealed that Mahurkar catheters carried 3.1 more risk of thrombosis than using central venous catheter.(Table 13,Figure 12).

Table (13): Comparisons of Central line types in different thrombotic outcomes.

Central line types	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.	Risk ratio
	No.	%	No.	%			
Central line	44	84.7%	8	15.3%	**0.05**	**S**	**3.1**
Mahurkar	18	64.3%	10	35.7%			

sig:significance,S:significant.



Figure(12)

- **Comparisons of different laboratory investigations in different study groups:**

There was statistically significant difference between study groups regarding kidney function test (urea, and creatinine), and also regarding hemoglobin level; with high mean of urea, and creatinine , and low mean of hemoglobin level were noted among patients who developed thrombosis.

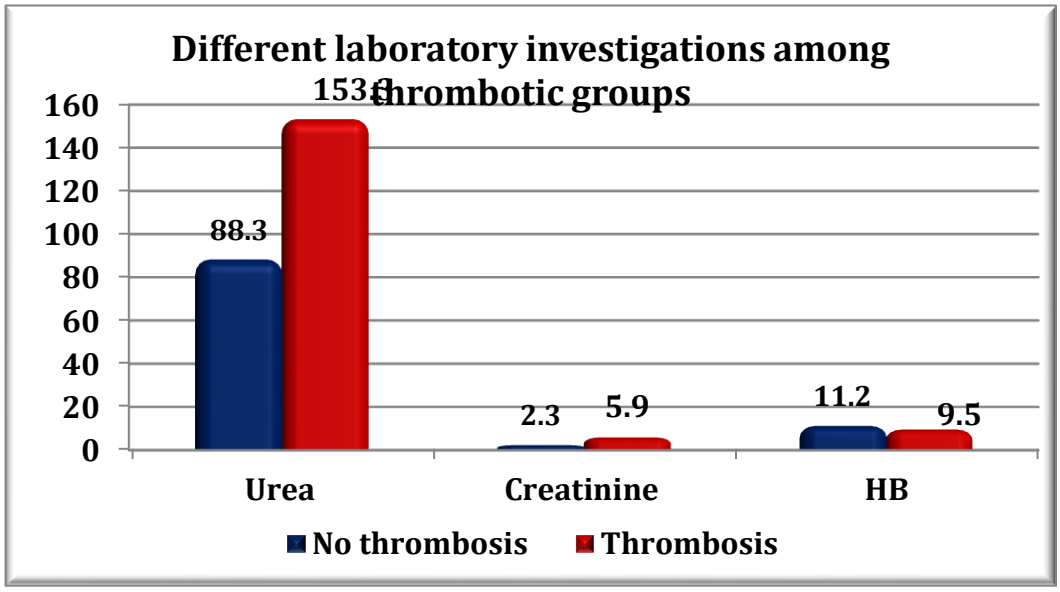
On the other hand there was no statistically significant difference regarding liver function test (ALS, and ALT) or INR level. (Table 14,Figure 13).

Table (14): Comparisons of different laboratory investigations in different study groups.

Variables	No thrombosis (number=62)		Thrombosis (number=18)		p-value	Sig.
	Mean	SD	Mean	SD		
kidney function tests						
Urea	88.3	46.4	**153.3**	60.7	**0.02**	**S**
Creatinine	2.3	1.4	**5.9**	3.8	**0.01**	**S**
Liver function tests						
ALT	39.8	20.4	39.2	29.1	0.3	NS

AST	34.5	26.4	26.4	23.9	0.2	NS
Other investigations						
INR	2.19	1.5	1.3	0.44	0.7	NS
HB	11.2	2.3	**9.5**	1.9	**0.004**	**HS**

SD:standard deviation,sig:significance,S:significant,NS:not significant, HS: highly significant.



DISCUSSION

Venous thromboembolism (VTE) remains a major cause of morbidity and mortality in ICU. **(Kekre N1 et al.,2018).**

The three factors of Virchow's triad—venous stasis,hypercoagulability, and changes in the endothelial blood vessel lining (such as physical damage) contribute to DVT.**(Altawan A et al.,2017)**

Upper extremity deep vein thrombosis (UEDVT) is an increasingly recognized complication in medical ICU, especially after the wide usage of central venous catheters (CVC) for different purposes.

(J ThrombHaemost., 2015).

There are many risk factors associated with upper extremity deep venous thrombosis following insertion of central venous catheters. These risk factors include lumen of catheter, infusate, and co-morbidities, such as congestive heart failure, renal failure, history of cancer, recent trauma, smoking, a history of prior deep vein thrombosis and recent surgery. **(Altawan A et al.,2017)**

Average length of hospital stay was almost doubled among patients developing UEDVT, 19.5 days, when compared to patients undergoing central line insertion without thrombosis, 10.8 days **(Thomas et al., 2012)**

Our study included 80 patients that were admitted at medical ICU with central venous catheter insertion for different purposes.

In our study we aimed to evaluate the incidence of CVC associated deep venous thrombosis.

All patients were subjected to full clinical history, physical examination, laboratory investigations and venous duplex imaging. Venous duplex was done before, 5th day and 10th day of insertion to detect venous thrombosis before clinical presentation of signs of thrombosis.

Deep venous thrombosis and risk factors:

- **Regarding age & sex:**

In our study we found that there was no statistically significant difference in the incidence of thrombosis between study groups regarding age and sex.

- **Regarding DM & HTN:**

In our study we found that there was no statistically significant difference in the incidence of thrombosis between study groups regarding HTN and DM.

This comes in contrast to**Debra Angelo et al., 2012;** where they found that incidence of thrombosis in diabetic patients is higher than that in non diabetic patients.

- **Regarding malignancy:**

We also found that there was statistically significant difference in the incidence of thrombosis between study groups regarding presence of cancers.

We found that incidence of thrombosis is higher in patients with malignancy representing (38.9%) versus (8.1%) with p value (0.004).

In agreement to our study,**Mansour A, Saadeh SS et al., 2018** in a study conducted on 87 patients with mean age of 52.4 found that the incidence of thrombosis is significantly higher in patients with malignancy than those without malignancy (45% vs. 17%).

Madabhavi I, Patel A,et al.,2018 reported that history of malignancy increases the incidence of thrombosis among patients with malignancy in a study included 352 patients with central venous catheter insertion for administration of chemotherapy.

We also found that there was statistically significant difference with p-value <0.05 between thrombosis groups as regards presence of bladder malignancy with higher percentage of thrombosis (16.7%) among patients with bladder cancer.

On the other hand there was no statistically significant difference with p-value >0.05 as regards other types of malignancies.

- **Regarding autoimmune diseases:**

We found that the incidence of thrombosis was increased in patients with autoimmune disease representing (27.8%) versus (4.8%) with p value (0.01).

This is in agreement with **Nikolova-Vlahova MK, Nikolov KV et al.,2015;** in their study which was conducted on 46 patients.16 of them were diagnosed with different autoimmune diseases such as(S.L.E.,anti phospholipid S and etc…) with increased incidence of thrombosis among patients with autoimmune diseases.

- **Regarding type of central line :**

We found that there was statistically significant difference in the incidence of thrombosis between study groups regarding type of central line with higher incidence among patients with mahurkar insertion (55.6%) versus (44.4%) among patients with central line insertion with P-value (0.05).

- **Regarding renal impairment:**

As regards renal impairment we found that there was statistically significant difference between study groups regarding presence of chronic kidney disease with higher percentage of thrombosis (27.8%) among patients with CKD with p value (0.002); which indicated the effect of CKD on thrombosis development.

Similarly **Lu HY, Liao KM,t al.,2018** in a study included 3564 ESRD patients after exclusion of patients with previous DVT, they found that incidence of thrombosis is substantially higher in the ESRD group than in the without-ESRD group (20.9% vs. 1.46%).

- **Regarding urea &creatinine:**

We found that there was statistically significant difference with p-value <0.05 between groups regarding kidney function test (urea and creatinine), with high mean of urea and creatinine among patients with thrombosis (153.3 and 5.9) versus (88.3 and 2.3) which indicated the effect of kidney function test on thrombosis development.

- **Regarding hemoglobin level:**

We also noted that there waslow mean of hemoglobin levelamong patients who developed thrombosis (9.5 gm\dl) versus (11.2gm\dl) with p value (0.004).

- **Regarding vasopressors:**

We found that there was statistically significant difference with p-value <0.05 between study groups regarding using vasopressor with higher percentage of thrombosis (55.6%) among patients who use

vasopressor versus (44.4%) among patients who didn't use vasopressors; which indicated the effect of vasopressor on thrombosis development.
On the other hand there was no statistically significant difference with p-value >0.05 regarding liver function test (ALS, and ALT) or INR level.
This difference between ourresults and their results may be due to our small sample size and short period of follow up.

CONCLUSION

- We can detect early thrombosis using venous duplex.
- Incidence of central line associated deep venous thrombosis increases in some co-morbidities like malignancy and autoimmune diseases.
- There was higher incidence of central line associated deep venous thrombosis in patients with large diameter catheters i.e. Mahurkars.
- Incidence of central line associated deep venous thrombosis also increases in patients with chronic kidney disease.
- The mean urea and creatinine among patients with thrombosis was higher.
- The mean hemoglobin levelamong patients who developed thrombosis was lower.
- There was higher incidence of central line associated deep venous thrombosis in shocked patient on vasopressors.

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