

## ORIGINAL RESEARCH

# To Assess the Factors Playing Role in Development and Outcome of Venous System Thrombosis

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Received: 26 December, 2020

Accepted: 15 February, 2021

### ABSTRACT

**Background:** Age and sex, obesity >30 Kg/m<sup>2</sup> increased the risk of thrombosis two-fold. The present study was conducted to assess the factors playing role in development and outcome of venous system thrombosis. **Materials & Methods:** A prospective observational cohort study design was adopted to assess the factors playing role in development and outcome of venous system thrombosis. The study was conducted among 100 patients. Various invasive and noninvasive radiological investigations and hematological investigations were done. **Results:** Of total 30 patients of CVST, 20 patients presented with headache and 10 patients had no headache which shows that 66% patients had headache. Out of 43 females, 55% cases were pregnant or in puerperium which was observed as major risk factor for development of venous thrombosis at various anatomical sites. Also, maximum patients had CVST as most common site of thrombosis in pregnancy and puerperium. In our study headache was most common symptom of CVT followed by nausea and vomiting. In DVT swelling and pain over affected limb was the most common symptom as it was observed in 49 among the 50 patients. For PVT pain abdomen and blood in vomitus and/or stool was most common symptom. Chest pain was observed in 11 patients of which 6 had DVT+PTE 2 had PTE and SVT and rest 1 patient had subclavian vein thrombosis. Among male patients, major risk factors for venous thrombosis is diabetes mellitus and smoking. **Conclusion:** The present study concluded that of a total of 30 patients of CVST, 20 patients were presented with headache. Out of 43 females, 55% cases were pregnant or in puerperium which was observed as major risk factor for development of venous thrombosis at various anatomical sites. Among male patients, major risk factors for venous thrombosis are diabetes mellitus and smoking.

**Keywords:** Headache, Pregnant, Puerperium, Venous Thrombosis.

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### INTRODUCTION

Except in thrombosis associated with surgery, examination of the thrombus in the human veins seldom indicates evidence of injury<sup>1</sup>, raising the question of how venous thrombosis is initiated. Venous thrombosis is believed to begin at the venous valves.<sup>2,3</sup> These valves play a major role in helping with blood circulation in the legs. They are also areas where stasis and hypoxia may occur. Direct evidence from autopsy studies and phlebography have established the venous valvular sinus as a frequent location of thrombosis initiation.<sup>1,4-6</sup> This phenomenon has been attributed to stasis, one of the components of Virchow's triad. Contrast media lingers in valve sinuses taking an average of 27 min to clear post-venography.<sup>7</sup> Valvular sinus stasis has also been associated with hypoxia and increased hematocrit<sup>8</sup>, constituting a potentially

hypercoagulable micro-environment. Furthermore, in animal models, oxygen tension drops very rapidly once blood flow is halted.<sup>8</sup> Abnormalities in these valves as a contributor to thrombotic risk have not been studied extensively at the molecular level. In a recent preliminary study, several of the important vessel based antithrombotic proteins, including thrombomodulin and endothelial protein C receptor (EPCR), were shown to be regionally expressed on the valves.<sup>9</sup> Furthermore, the expression of these proteins showed considerable inter-individual variation. Since expression of these anticoagulant proteins is sensitive to the environment, either hypoxia or inflammation could lead to down regulation, possibly contributing to the initiation of thrombosis.<sup>10-12</sup> In addition, hypoxia can lead to up-regulation of procoagulant activity including tissue factor on endothelium.<sup>11,12</sup> After correcting for age and

sex, obesity >30 Kg/m<sup>2</sup> increased the risk of thrombosis two-fold.<sup>13</sup> Like oral contraceptives<sup>14</sup>, pregnancy carries an increased risk of developing venous thrombosis<sup>15</sup> that is increased still further in patients with thrombophilia. This increased risk is present in all trimesters of pregnancy and in the post-partum period. Potential contributing factors might be disturbed blood flow and hormonal changes.<sup>15</sup> The present study was conducted to assess the factors playing role in development and outcome of venous system thrombosis.

## MATERIALS & METHODS

A prospective observational cohort study design was adopted to assess the factors playing role in development and outcome of venous system thrombosis. The study was conducted in the department of general medicine at RNT Medical College, Udaipur. The protocol was submitted before the initiation of study and was approved by the Institutional Review Board and Ethics Committee. Informed consent was obtained from all the participants prior to their entry into the study. The study was conducted among 100 patients admitted and diagnosed with venous system thrombosis. Patients admitted and diagnosed with venous system thrombosis with age >18 years, pulmonary vein thrombosis, deep venous thrombosis, cerebral venous thrombosis, venous sinus thrombosis, superior vena cava thrombosis, inferior vena cava thrombosis, Portal vein thrombosis were included in the study. Alcoholics, trauma, superficial thrombophlebitis, patient/caregiver refusing consent for entering the study, patient already on therapeutic anticoagulation, e.g.: prosthetic heart valves, stroke hemorrhagic, arterial infarction, Eclampsia were excluded from the study.

## DATA COLLECTION

All the variables of interest were collected through a data abstraction form which was duly filled in by the principal investigator (self) on day 1 of admission. The predictor variables related to treatment and outcomes were filled, just prior to the patient exiting the study. All the variables used in the data abstraction form were clearly defined prior to starting the study, to avoid discrepancies and ambiguity. Various invasive and noninvasive radiological investigations and hematological investigations were done according to patients' profile, signs and symptoms. This was done by principal investigator (self). The patients were followed up till the time of discharge and hospital outcomes. The primary outcome of the study was to assess the factors playing role in development and outcome of venous system thrombosis.

## STATISTICAL METHODS

Analysis was done using SPSS version 16 (Copyright 2007). Data was entered into EPIDATA software with

quality control checks such as range and consistency. Data quality was further explored using histogram, Box Cox plots and frequency distributions (which was used for continuous variables). Categorical variables have been presented as numbers and percentages and continuous variables as mean and standard deviation (SD). Logistic regression analysis was done to determine the risk factors Venous thrombosis with log link. Model assumptions were checked using likelihood residual plots against predicted probability. Goodness of fit of the model was assessed using Hosmer Lemeshow chi-square statistics.

## RESULTS

Among male most patients were from 31-50 years age group and among females most of them from 18-30 years age group. The mean age was 24 years. Male predominance for venous thrombosis was found in the study and 66% patients were males and 34% patients were females. Male to female ratio was 2:1. Of the 100 patients enrolled in the study there was 1 case of subclavian vein thrombosis and 3 cases of superior venacava thrombosis. Rest maximum cases were either DVT or CVST. None of the patients were presented with IVC thrombosis. All of them underwent all investigations as per protocol and also there was no mortality. In our study, the maximum cases were DVT i.e. 50% followed by CVST i.e. 30% followed by PVT and SVT. Among males' maximum patients had DVT I.E. 50% among females maximum patients had CVST i.e. 30%.

Of total 30 patients of CVST, 20 patients were presented with headache and 10 patients had no headache which shows that 66% patients had headache.

In our study, out of 43 females, 55% cases were pregnant or in puerperium which was observed as major risk factor for development of venous thrombosis at various anatomical sites.

Also, maximum patients had CVST as most common site of thrombosis in pregnancy and puerperium.

In our study headache was the most common symptom of CVT followed by nausea and vomiting.

In DVT swelling and pain over affected limb was the most common symptom as it was observed in 49 among the 50 patients.

For PVT pain abdomen and blood in vomitus and/or stool was the most common symptom.

Chest pain was observed in 11 patients of which 6 had DVT+PTE 2 had PTE and SVT and rest 1 patient had subclavian vein thrombosis.

Among the study population 17% of patients had diabetes mellitus and 17% of patients were smokers.

Among male patients, major risk factors for venous thrombosis are diabetes mellitus and smoking. In our study it was observed that major risk factor among female population was pregnancy and puerperium for the development of venous thrombosis as seen in 55% female patients.

Moreover, it was observed that 12% of patients had hypertension.

Among infectious causes, tuberculosis was the most common cause of thrombosis followed by Hepatitis B infection.

11% of patients had venous thrombosis post-surgery and 6% patients had dehydration being risk factors for thrombosis.

Also 8% of patients had CKD and nephritic syndrome was seen in 4% patients.

Rest other comorbidities identified in our study were OCP USE, CVA and connective tissue disease like APLA which was identified in 5% patients.

**Table 1: Patient of CVST presenting with headache (n=30)**

Headache present	Headache absent	Total
20	10	30

**Table 2: Correlation of pregnancy and puerperium with venous thrombosis**

Anatomic site of venous thrombosis	Pregnant/ puerperium	Non pregnant female	Total female cases
CVST	12	4	16
DVT	4	6	10
PVT	0	2	2
Subclavian vein thrombosis	0	0	0
DVT+PTE	2	1	3
PTE	1	1	2
SVT	0	1	1
Total	19	15	34

**Table 3: Major symptoms of Venous thrombosis (n=100)**

Symptoms	CVST	DVT	PTE	DVT+PTE	Subclavian vein thrombosis	SVT	PVT
Headache	20	0	0	0	0	0	0
Vomiting	19	0	0	0	0	0	0
Seizures	17	0	0	0	0	0	0
Altered sensorium	18	1	0	0	0	0	0
Focal neurological deficit	12	0	0	0	0	0	0
Hemianopia	3	0	0	0	0	0	0
Fever	9	7	0	0	0	1	0
Dyspnea on exertion	0	0	2	6	0	2	0
Chest pain	0	0	2	6	1	2	0
Swelling over neck	0	1	0	0	1	2	0
Swelling and/or pain in affected limb	0	49	0	6	0	0	0
Pain abdomen	0	1	0	0	0	0	8
Blood in vomitus and/or stool	0	0	0	0	0	0	6

**Table 4: Risk factors and comorbidities in study population (n=100)**

Risk factors and comorbidities	No. of patients	Male	Female	%
Diabetes mellitus	17	12	5	17
Hypertension	12	8	4	12
Smoking	17	17	0	17
Hyperhomocystenemia	5	5	0	5
Chronic liver disease	6	4	2	6
COPD	2	2	0	2
Venous catheterization	1	1	0	1
OCP use	2	0	2	2
CVA (stroke)	1	1	0	1
Dehydration	6	4	2	6
Post surgery	11	11	0	11
Pregnancy and puerperium	19	0	19	19
CTD (APLA,SLE,RA)	5	0	5	5

<b>Chronic kidney disease</b>	8	3	5	8
<b>Nephritic syndrome</b>	3	2	1	3
<b>Infections</b>	<b>TB</b>	4	0	4
	<b>HIV</b>	1	0	1
	<b>Hepatitis B</b>	3	2	1
	<b>Malaria</b>	1	0	1
	<b>Scrub typhus</b>	1	1	0
<b>Malignancy</b>	5	3	2	5

## DISCUSSION

Among patients hospitalized for acute medical illness, active cancer is a major venous thromboembolism risk factor. After controlling for cancer, additional independent risk factors for venous thromboembolism within three months after hospitalization for acute medical illness include increasing age and BMI, neurological disease with leg paresis, fracture, chronic renal disease, central venous catheter, prior superficial vein thrombosis, and prolonged immobility.<sup>16</sup> Petrauskienė V et al<sup>17</sup> stated that Diabetes mellitus is a reported risk factor for VTE and pulmonary embolism (PE), similarly in our study diabetes was found risk factor in 17% patients. This could also be explained by the fact that persons with diabetes are frequently hospitalized for major surgery or acute medical illnesses or confined to a nursing home or chronic rehabilitation facility.

Semrad TJ et al<sup>18</sup>, stated patients with hypertension have been found with 2-fold increased likelihood of developing DVT. Similarly in our study population also hypertension was identified as major risk factor in 12% population.

A study by Brown HL et al<sup>19</sup> stated the risk of venous thromboembolic events has been reported to be in the range from 7 to 25 per 10,000 pregnancies and is highest around delivery, when the risk is more than 20-fold greater than that of non-pregnant women. Our study also identified pregnancy and puerperium as a major risk factor in 55% females of study population. Goldhaber SZ et al<sup>20</sup>, identified smoking as independent risk factor for venous thrombosis similarly our study also identified smoking as risk factor in 17% of study population.

Azin et al<sup>21</sup> studied 61 patients with CVST where male to female ratio was 1:3.1. Headache was seen in 91.8% of the patients. Similarly in our study, headache and altered sensorium were most common presenting symptoms.

## CONCLUSION

The present study concluded that of a total of 30 patients of CVST, 20 patients were presented with headache. Out of 43 females, 55% cases were pregnant or in puerperium which was observed as major risk factor for development of venous thrombosis at various anatomical sites. Among male patients, major risk factors for venous thrombosis are diabetes mellitus and smoking.

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