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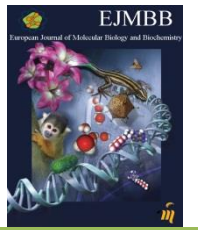

INFLAMMATORY MARKERS IN CRITICALLY ILL PATIENTS WITH VENOUS THROMBOSIS – A TERTIARY HOSPITAL-BASED STUDY

Dr. Shaheen B Shaikh*[1], Dr. Ismail H M[2], Dr. Bhavya R[3], Dr. Ganesh P[4], Sarfaraz Shaikh[5]

[1]Associate Professor, Department of Biochemistry, Yenepoya Medical College Hospital, Mangaluru, Karnataka, India,
[2]Associate Professor, Department of Critical Care Medicine, Yenepoya Medical College Hospital, Mangaluru, Karnataka, India.
[3]Senior Resident, MVJ Medical College and Research Hospital, Hoskote Taluk, Bangalore Rural .mail
[4]Professor and Head, Department of Biochemistry, Yenepoya Medical College Hospital, Mangaluru, Karnataka, India.
[5]Consultant, Department of Emergency Medicine, DM WIMS Medical College Wayanad, Kerala, India.

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ABSTRACT

Objectives -Vein Thrombosis represents a major public health problem, exacting a significant human and economic toll on the Nation. Venous thrombosis is an important and possibly preventable cause of morbidity and mortality in hospitalized patients. The objective of this study was to analyze the inflammatory markers in venous thrombosis. Materials and Methods- A cross-sectional study was conducted on patients admitted to tertiary Hospitals. The study was conducted on 59 radiographically confirmed cases of venous thrombosis. Informed written consent was obtained for participation in the study and conduction of investigations. The study was conducted between the period of November 2017 and September 2019. Results- The mean age of the study group was 43.6 years (SD= ±16.4) ranging from 20 to 72years. Out of the 59 patients, 48 were males (81.4%) and 11 were female (18.6%). The mean Body mass index of the patients was 24.33 ± 2.84 kg/m2. Among 59 patients, 48 patients (81.3%)had elevated CRP. 46 patients (77%) had elevated Serum Homocysteine levels(>15µmol/L). Among 59 participants 74.6 % had low HDL, 61% had High LDL, 45% had high Triglycerides. Total Cholesterol was elevated by 40.7 %. D dimer levels were elevated in 98. 3 %. Conclusion- We conclude that unprovoked venous thrombosis is a common problem among patients 20-29 yrs, male gender, BMI> 25 kg/m2 presenting to tertiary care hospital. Inflammatory markers were significantly elevated in venous thrombosis.

Corresponding Author

Dr. Bhavya R MBBS, MD
Email: - drshaheenshaikh@yenepoya.edu.in

Introduction

Deep Vein Thrombosis and Pulmonary Embolism (DVT/PE) represent a major public health problem, exacting a significant human and economic toll on the Nation. In the past decade, deep vein thrombosis has increasingly been recognized as an important and possibly preventable cause of morbidity and mortality in hospitalized patients.[1]Understanding the natural history of venous thrombosis is important for optimal management of this condition. Once risk factors are recognized it is possible to avoid these risk factors or to use active prophylaxis to reduce morbidity and mortality.[2] The overall age- and sex-adjusted annual incidence of VTE was 1.17 per 1,000 (48 per 1,000 for DVT and 69 per 1,000 for PE). [2] According to US Census Bureau, the population of approximately 300 million Americans suggests that more than 350,000 individuals are affected by DVT/PE each year.[3]

Extrapolating to today's population suggests that an estimated 28,200 people die each year from this disease. Many of those who survive will be affected for the rest of their lives[4]. Most cases of venous thrombosis can be identified and be prevented well in advance with adequate prophylaxis to prevent the post-thrombotic sequelae and complications associated with venous thrombosis[5] . Hence it is important to be aware of risk factors, course, and biomarkers of venous thrombosis, as early diagnosis and treatment can prevent life-threatening complications and give a better outcome. Hence we conducted this study intending to analyze the inflammatory markers in venous thrombosis.

MATERIALS AND METHODS:

A Cross-sectional study was conducted on patients admitted to the Tertiary Hospital Critical care department. The study was conducted between the period of November 2017 and September 2019. The study was conducted on 59 radiographically confirmed Diagnosed cases of Deep vein thrombosis, Pulmonary thromboembolism, Cerebral venous thrombosis, Portal and splenic vein thrombosis was detected by radiographic imaging like Doppler ultrasonography, Computerized Tomography/ MR Venogram. Informed written consent was obtained for participation in the study and conduction of investigations. Clinical data, Case history including personal history, comorbid illness, and physical examination was done. With informed consent, blood samples were collected from patients with deep vein thrombosis. The venous blood samples from all subjects were collected under aseptic precautions and sent for a complete Haemogram study, ESR, CRP, peripheral blood smear, Lupus anticoagulant work up, and serum Homocysteine levels.

STATISTICAL ANALYSIS

The data was documented on a master chart. Descriptive statistical analysis has been carried out in the present study. Collected Data was summarized by frequency and percentage and represented in the form of Diagrams. Inferential methods such as Fisher Exact test were used to compare. The continuous variables were expressed as mean ± standard deviation. The categorical variables were expressed as percentages and compared by the chi-square test. Analysis was performed by SSP17 software and a P value less than 0.05 considered as significant.

RESULTS

A total of 59 patients who were admitted with a diagnosis of venous thrombosis in the critical care unit were included in the study. Out of 59 participants, 17 (28.8%) were in the age group of 20-29yrs, 4 (6.77%) in the age group of 30-39yrs, 14 (23.7%) in the age group of 40-49yrs, 10 (16.9%) in the age group of 50-59, 8 (13.55%) in the age of 60-69 years and 6 (10.1%) in the age group of 70 -79 years. The mean age of the study group was 43.6 years (SD= ±16.4) ranging from 20 to 72 years. Out of the 59 patients, 48 were males (81.4%) and 11 were female (18.6%). The mean Body mass index of the patients was 24.33 ± 2.84 kg/m^2.

Among 59 patients 37 participants (62.71%) presented with deep vein thrombosis of limbs. 12 patients (20.3%) presented with cortical venous thrombosis,5 patients had a pulmonary embolism.

Among 59 patients, 48 patients (81.3%) had elevated CRP. The mean CRP level was 16.66. All patients underwent Serum Homocysteine level estimation, of which 46 patients (77%) had Elevated Serum Homocysteine levels(>15µmol/L). Among 59 participants 74.6 % had low HDL, 61% had High LDL, 45% had high Triglycerides. Total Cholesterol was elevated by 40.7 %. D dimer levels were elevated in 98. 3 %. Among 59 patients 12 (20.3%)had polycythemia, which was defined by a Haemoglobin level of>17 mg/dl and by peripheral smear reports, and 11patients were Anemic with Haemoglobin <10 mg/dl. The mean Hemoglobin was 13.2mg/dl (SD±7.07). 38 patients,64 % had elevated ESR. The mean Erythrocyte sedimentation rate (ESR) was 33.45.

DISCUSSION

This was a study on 59 patients with venous thrombosis presenting to a teaching medical hospital to analyze inflammatory markers of these patients The results of our study showed that nearly one-third of these patients belonged to age group 20-30 years with the second biggest group being in the age group 40 -50 years and nearly 80 percent were males.

This indicates that these patients did not have traditional risk factors such as pregnancy, puerperium, and hormonal contraceptive use or comorbidities such as immobilization which often are risk factors in females.

Similar observations were made by Silverstein, John Heit JA et al [6] who conducted a 25-year population-based, retrospective study of the incidence of Deep vein thrombosis and pulmonary embolism involving 2218 patients, incidence was higher in males. Male: female ratio was 1.2:1 and the mean age was 61.7 ± 20.4 years.

The majority of our cases(nearly 60%) were deep vein thrombosis, followed by cerebral venous thrombosis(20 %). Pulmonary embolism and visceral thrombosis occurred less commonly in our series. This is probably because we included patients mainly referred to the medical department. In comparison with a similar study by Cheena Garg et al [7] among the total of 622 patients, 26 suffered from venous thrombosis, Eleven patients (58%) had deep vein thrombosis and 8 patients (42%) had pulmonary thromboembolism and 7patients(26.9%) patients had CVT.

Our study showed that nearly 45% had high BMI, however, it did not emerge as a risk factor for venous thrombosis in general, but emerged as a risk factor for deep vein thrombosis and CVT, and pulmonary embolism. A

study by Paul Dstein, Afzal Beemath etal[8] 21-year population-based study in a population, Among 1,89, 25,000, patients 1,20,15,000 patients diagnosed with obesity, of which (0.76%) had a pulmonary embolism. Deep vein thrombosis was diagnosed in 2.02% diagnosed with obesity. The relative risk of deep venous thrombosis, comparing obese patients with non-obese patients, was 2.50(95% confidence interval [CI] = 2.49-2.51). The relative risk of pulmonary embolism was 2.21 (95% CI = 2.20-2.23). Obese females had a greater relative risk for deep venous thrombosis than obese males, 2.75 (95% CI = 2.74-2.76) versus 2.02 (95% CI = 2.01-2.04).Obesity had the greatest impact on both men and women aged less than 40 years.

In our study patients (27%) patients had a history of Diabetes, (30.5%) patients had HTN. In our, study Diabetes was significantly associated with pulmonary embolism. A similar study was done by Gregory Piazza etal[9] in 2012, among 2488 cases of venous thrombosis 476 had diabetes was associated with a significant increase in the risk of recurrent deep vein thrombosis (adjusted odds ratio [AOR] 1.74; 95% confidence interval [CI], 1.21–2.51). In our study, APLA was identified as a risk factor in 2 patients. In our study, 78% had high Serum Homocysteine levels (>15µmol/L). This emerged as a risk factor for all venous thrombosis and CVT. However, we do not have data on the population prevalence of hyperhomocysteinemia. Low fruits and vegetable consumption causing folate deficiency, low diary and nonvegetarian food consumption causing Vitamin B 12 deficiency combined with genetic factors could have been responsible.

In a study conducted by Paolo Simion, Paolo Prandoni etal[10] 60 patients (28.8%) had Hyperhomocysteinemia. The odds ratio for having an acute DVT in patients with Hyperhomocysteinemia was 2.6 (95% Cl: 1.1-5.9). The preliminary results of the present study showed that inflammation may be connected to the pathogenesis of Venous Thrombosis. The CRP and ESR values were significantly higher in VT patients in this study. Several previous studies have been performed to show the positive linear relationship between inflammation and venous thrombosis in recent years[11-13]. They have been investigated in several studies and elevated levels were shown to be important biomarkers in coronary artery diseases[14,15] Harvey et al.[16] stated that low-grade inflammation, assessed by measurement of CRP, was associated with the risk of venous thrombosis. In our study, around 81% had elevated CRP and it was associated with all venous thrombosis in general and DVT in particular, suggesting that inflammation could have triggered thrombosis or thrombosis could have triggered inflammation. In a resource-limited setting where D Dimer tests are unavailable CRP could be used as a biomarker.

Table 1. Laboratory parameters and their association with venous thrombosis

Lab Parameters	Present	Number of Patients	Percentage (%)	Significance
ESR >20 mm/hr		38	64.4 %	0.036
CRP >3mg/L	Yes	48	81%	0.000
D Dimer>500ng/ml	Yes	58	98.3%	0.000
Triglyceride.>150 mg/dl	Yes	27	45.8%	0.603
HDL<40 mg/dl	Yes	44	74.6%	0.000
LDL >100mg/dl	Yes	36	61%	0.117
Total cholesterol .> 200 mg/dl	Yes	24	40.7 %	0.193
APLA	Yes	2	3.4%	0.000
Serum Homocysteine>15 µmol/L	Yes	46	78%	0.000
Polycythemia	Yes	12	20.3 %	0.000
Iron deficiency Anaemia	Yes	11	18.6%	0.000

P< 0.05 was considered a significant

Table 2. Laboratory parameters and their association with DVT

Lab parameters	Present	Number of patients	Percentage	Significance
ESR >20mm/hr	Yes	24	64.9 %	0.924
CRP >3 mg/L	Yes	33	89.2%	0.045
D- DIMER >500ng/ml	Yes	37	100%	0.191
Triglyceride >200mg/dl	Yes	18	48.6%	0.564
HDL <40mg/dl	Yes	29	78.4%	0.384
LDL >100mg/dl	Yes	23	62.2%	0.815

Total Cholesterol >200mg/dl	Yes	20	54.1%	0.007
APLA	Yes	1	2.7%	0.705
Serum Homocysteine>15 µmol/L	Yes	27	27%	0.230
Polycythemia	Yes	16	43.24 %	0.000
Iron deficiency Anemia	Yes	9	24%	0.000

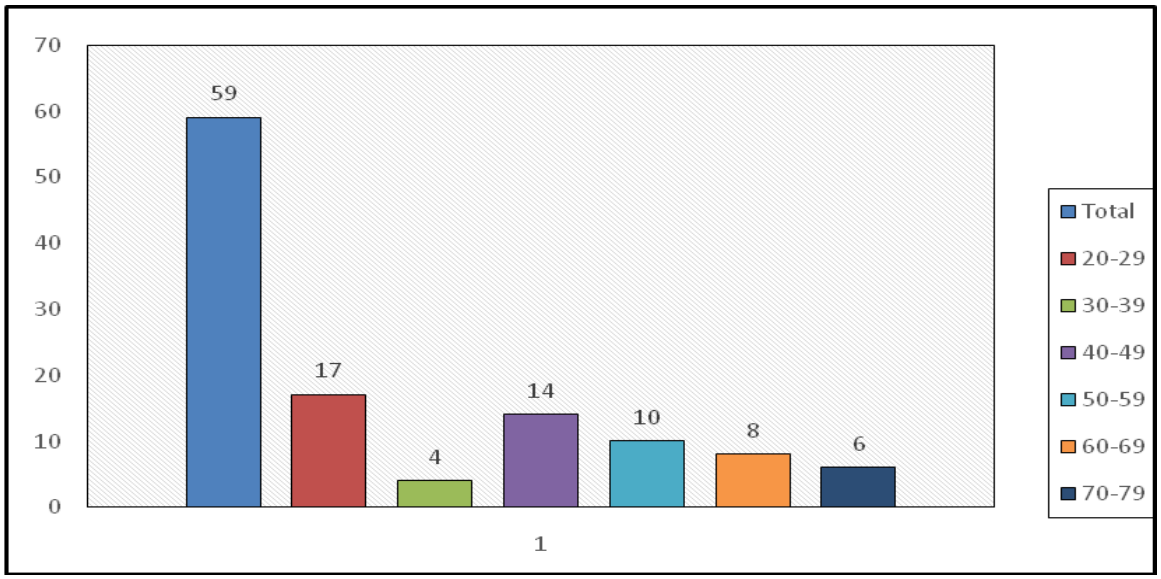
P< 0.05 was considered a significant

Table 3. Lab parameters and their association with CVT

Lab parameters	Present	Number of patients	Percentage	significance
ESR >20mm/hr	Yes	8	66.7 %	0.855
CRP >3mg/L	Yes	7	58.3%	0.022
D- DIMER >500ng/ml	Yes	1	8.3%	0.046
Triglyceride >200mg/dl	Yes	4	33.3	0.333
HDL <40mg/dl	Yes	8	66.7 %	0.481
LDL >100mg/dl	Yes	9	75%	0.266
Total Cholesterol >200mg/dl	Yes	4	33.3%	0.562
APLA	Yes	1	8.3%	0.289
Serum Homocysteine>15 µmol/L	Yes	12	100 %	0.039
Polycythemia	Yes	3	25%	0.000
Iron deficiency Anemia	Yes	2	16%	0.000

P< 0.05 was considered a significant

Fig 1. Age Distribution of Patients Studied



CONCLUSION

We conclude that unprovoked venous thrombosis is a common problem among patients 20-29 yrs, male gender, BMI> 25 kg/m2 presenting to tertiary care hospital. Inflammatory markers were significantly elevated in venous thrombosis

Among critically ill hospitalized patients, baseline inflammatory markers were independently associated with Venous thrombosis, suggesting a prognostic role for inflammation in venous thrombosis prediction.

Limitations of Study

- Small study population
- Cross-sectional study with no controls.

Conflict of Interest – No

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