HOW TO CITE THIS ARTICLE:

ABSTRACT: Thrombophilia is a disorder characterized by an increased incidence of venous and arterial thrombosis. It may be hereditary or acquired. Protein C and Protein S deficiency with or without high Homocysteine levels have been reported to be associated with thrombogenic events. AIM: To find protein C, protein S deficiency and hyperhomocysteinemia as the risk factors for thrombogenic events through a retrospective analysis of patients admitted in the medicine department with thrombogenic events over a period of 1 year were evaluated. MATERIALS AND METHODS: Total 15 patients with thrombogenic events were reviewed for the demographic data, history, clinical findings and investigation reports. The data analyzed to find the risk factors associated. Protein C, Protein S and Homocysteine levels were evaluated on a fully automated coagulometer. Acquired causes of were excluded. RESULTS: Average age of the patient was 31.8 years with male predominance in 67%. Thrombogenic events was mainly in the form of cerebrovascular accidents in 40% (6 of 15) patients and deep vein thrombosis in 26.7 %( 4 of 15) patients. Protein C deficiency occurred in 46.7% (7 of 15) patients, while Protein S deficiency in 86.7 % (13 of 15) patients. Combined Protein C and S deficiency occurred in 40% (6 of 15) patients. Hyperhomocysteinaemia was documented as a predisposing factor in 26.7 %( 4 of 15) patients. CONCLUSION: We conclude that, the frequency of protein C deficiency, protein S deficiency and hyperhomocysteinemia are significantly higher among those with thrombogenic events than general population and hence need to be screened for in all thrombogenic events.

INTRODUCTION: Thrombophilia is a disorder characterized by an increased incidence of venous and arterial thrombosis. It may be hereditary and conferred by genes inherited from one or more parents, or it may be acquired through situations such as surgery, cancer, pregnancy, or certain medications (eg, some contraceptive and menopausal hormone replacement products). The two most common hereditary thrombophilia conditions are the factor V Leiden and prothrombin 20210 gene mutations. [1,2] Protein C and Protein S deficiency with or without high Homocysteine levels have been reported to be associated with thrombogenic events. Hence, a retrospective study of thrombogenic events in patients admitted in medicine department was done to find protein C, protein S deficiency and Homocysteine levels as associated risk factors for the same.

AIM: To find protein C, protein S deficiency and hyperhomocysteinemia as the risk factors for thrombogenic events among patients admitted in medicine department.

Design: A retrospective analysis of 15 cases admitted in the medicine department of teaching institute with thrombogenic events over a period of 1 year were evaluated for inherited thrombogenic disorders.
MATERIALS AND METHODS: The records of 15 patients with thrombogenic events were reviewed for the demographic data, history, clinical findings and investigation reports. The data was then analyzed to find the risk factors associated and the significance of the same. Protein C, Protein S and Homocysteine levels were evaluated on a fully automated coagulometer. Family studies for protein C and/or S deficiency were not performed as not all patients with this deficiency will experience episodes of thrombosis and low levels of either factor by itself in asymptomatic patients are not an indication for anti coagulation. Acquired causes of thrombophilia like pregnancy, postpartum period, surgery, post operative state, immobilization, obesity, malignancy, nephrotic syndrome, myeloproliferative disorders, paroxysmal nocturnal hemoglobinuria, hyperviscosity and drugs like oral contraceptives were excluded. Informed consent was obtained in all patients and local ethical committee approval obtained.

RESULTS: Average age of the patient was 31.8 years (range 20 to 40 years) with male predominance in 67% (10 of 15) and 33%(5 of 15 ) were females (table-1).

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of patients</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>21-30 years</td>
<td>6</td>
<td>40</td>
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<tr>
<td>31-40 years</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>&gt;40 years</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of patients</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10</td>
<td>67</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>33</td>
</tr>
</tbody>
</table>

Table-1: Demographic data and thrombogenic events

Thrombogenic events was mainly in the form of cerebrovascular accidents in 40% (6 of 15) patients and deep vein thrombosis in 26.7 %(4 of 15) patients as depicted in table-2.

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>No.of patients</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebro vascular accidents</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>Cortical vein thrombosis</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Popliteal artery thrombosis</td>
<td>1</td>
<td>6.6</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>1</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Table-2: Thrombogenic events

Protein C deficiency occurred in 46.7% (7of 15) patients (table-3), while Protein S deficiency in 86.7 %(13 of 15) patients (table-4). Combined Protein C and S deficiency occurred in 40% (6 of 15) patients. Hyperhomocysteinaemia was documented as a predisposing factor in 26.7 %(4 of 15) patients (table 5).
**DISCUSSION:** Thrombophilia can be defined as a predisposition to form clots inappropriately. Thrombotic events are increasingly recognized as a significant source of mortality and morbidity. The predisposition to form clots can arise from genetic factors, acquired changes in the clotting mechanism or more commonly, an interaction between genetic and acquired factors.

Inherited thrombophilia is a genetic tendency to venous thromboembolism. The Factor V Leiden and prothrombin gene mutations are the most common causes of the syndrome accounting for more than 50 percent of cases. Deficiencies in protein S, protein C, and antithrombin account for most of the remaining cases, while rare causes include the dysfibrinogenemias.

Incidence of clinically symptomatic protein C deficiency lies between 1:16,000 to 1:32,000 persons while that of symptomatic protein S deficiency is 1:20,000. Hyperhomocysteinemia can be precipitated by both genetic defects and acquired medical conditions, including vitamin deficiency states.

Average age of the patient was 31.8 years (range 20 to 40 years). Family studies from the Netherlands and the US have shown that family members who are Protein C deficient are at an 8–10 fold increased risk of venous thrombosis, and, by age 40, 50% or more will have experienced a thrombotic event. Male predominance was evident in 67% (10 of 15) and 33% (5 of 15) were females. In 1987, Engesser and colleagues conducted a study on 12 Swedish families with 136 members and found 71 of them to be heterozygous for Type I protein S deficiency; 55% of those who carried the defect were found to have had a thrombotic event and 77% of those were recurrent. About half of the cases were precipitated by another condition. They also showed that in phenotypic protein S deficient families, the likelihood that affected family members remain thrombosis-free at 45 years of age was 35 to 50 percent. This study showed a difference in rates between men and women but was not able to provide an adequate explanation in terms of difference in risk factors.
between the two sexes. [10] In the present study, thrombogenic events was mainly in the form of cerebrovascular accidents in 40% (6 of 15) patients and deep vein thrombosis in 26.7 % (4 of 15) patients. Venous thrombosis dominated, with deep vein thrombosis being most common manifestation, followed by cerebral venous thrombosis. A single case of portal and splenic vein thrombosis was detected. An association of deficiencies in protein C or protein S and venous thromboembolism is well documented. [11-15] Of the arterial thrombosis, cerebral artery occlusion causing hemiplegia was the commonest manifestation. A single case of peripheral artery occlusion was diagnosed. Protein C deficiency occurred in 46.7% (7 of 15) patients, while Protein S deficiency in 86.7 % (13 of 15) patients. Combined Protein C and S deficiency occurred in 40% (6 of 15) patients. Protein S was the commonest predisposing cause for both arterial and venous thrombosis with Protein C being less common. Combined deficiency of protein C and protein S is rare and only few confirmed cases with genetic decoding has been reported. [16, 8]

Hyperhomocysteinaemia was found as an additional risk factor in 26.7 % (4 of 15) patients.

CONCLUSION: We conclude that, the frequency of protein C deficiency, protein S deficiency and hyperhomocysteinemia are significantly higher among those with thrombogenic events than general population and hence need to be screened for in all thrombogenic events.

REFERENCES:

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