Recent studies suggest that mild hyperhomocysteinemia may be a risk factor for venous thromboembolic disease (VTED). In this work we evaluated the prevalence of moderate hyperhomocysteinemia in patients with VTED in our area. We found hyperhomocysteinemia in 23.4% of 64 patients studied compared with 7.35% of 68 healthy controls (p=0.014). Our results suggest that moderate hyperhomocysteinemia is one of the most prevalent abnormalities associated with VTED.

Several studies have concluded that moderate hyperhomocysteinemia is an independent risk factor for atherosclerosis and arterial occlusive diseases in the general population. Recent studies suggest that mild hyperhomocysteinemia may also be a risk factor for venous thromboembolic disease (VTED) and its recurrence. The objective of this study was to evaluate whether VTED is associated with an increased prevalence of hyperhomocysteinemia in our area. Sixty-four consecutive unrelated Spanish patients with objectively diagnosed VTED (31 females and 33 males, mean age 52.16±15.70) and sixty-eight healthy controls (41 females and 27 males, mean age 46.6±10) were studied in our Institution, between January 1996 and December 1996. The assessment of hyperhomocysteinemia was performed by measuring the concentration of fasting plasma homocysteine and its increase 6 hours after oral methionine loading (PML) (0.1 g L-methionine/kg body weight). Concentrations of plasma homocysteine were determined by high-performance liquid chromatography and fluorescence detection. In order to investigate other biological abnormalities causing thrombophilia, we also determined: antithrombin, plasminogen and amidolytic protein C by chromogenic substrates; anticoagulant activity of protein C; total protein S and free protein S by the ELISA method; antiphospholipid antibodies by ELISA; and the factor V Leiden mutation by standardized methods. Hyperhomocysteinemia was defined as fasting plasma homocysteine levels and/or PML absolute increments above the 95th percentile of the level in the control group (respectively 11.43 µmol/L and 28.72 µmol/L). Hyperhomocysteinemia was detected in 15 patients (23.4%, IC 95% 13.0-33.8), eight females and seven males (mean age 63.18±8.65 yrs) and 5 subjects in the control group (7.35%) (p=0.014). Malignancies were 13 times more frequent in patients with hyperhomocysteinemia than in patients without it. Although the mechanisms underlying this association are unclear, higher plasma homocysteine in patients with cancer has been noted before. It would be interesting to perform more studies to clarify the association between hyperhomocysteinemia and VTED in cancer patients.

Within the group of patients who had had at least one objectively diagnosed VTED, the age at first event was lower in patients without hyperhomocysteinemia than in patients with hyperhomocysteinemia (42.08±15.41 years compared with 52.46±8.13 years; p<0.05). Recurrences and family history of VTED were more frequent in patients with hyperhomocysteinemia than in patients without hyperhomocysteinemia, but differences were not significant. As for other deficiencies, two patients of the hyperhomocysteinemia group had antiphospholipid antibodies, whereas two patients of the non-hyperhomocysteinemic group had factor V Leiden mutation while another had activated protein C resistance without factor V Leiden mutation. Hyperhomocysteinemia did not seem to add to the thrombotic risk of oral contraceptives (Table 1).

This study is the first report on the prevalence of hyperhomocysteinemia in a Spanish population with VTED. It was present in about 23% of patients with VTED and our results suggest that moderate hyperhomocysteinemia is a common biologic abnormality in these individuals. We are, therefore, of the opinion that homocysteine assessment should be included in the laboratory evaluation of patients with VTED. Measurements of fasting plasma homocysteine and post-methionine levels should be performed because the detection of hyperhomocysteinemia is one of the most prevalent abnormalities associated with VTED.

### Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Total patients</th>
<th>No HH</th>
<th>HH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>64</td>
<td>49</td>
<td>15</td>
</tr>
<tr>
<td>Mean age ±SD</td>
<td>52.1±15.70</td>
<td>49.64 ±15.91</td>
<td>63.18 ±8.65 (p&lt;0.05)</td>
</tr>
<tr>
<td>Female:male ratio</td>
<td>33/31</td>
<td>25/24</td>
<td>8/7 (n.s)</td>
</tr>
<tr>
<td>Family history of VTED</td>
<td>25 (39.06%)</td>
<td>19 (38.77%)</td>
<td>8 (53.33%) (n.s)</td>
</tr>
<tr>
<td>Recurrent VTED</td>
<td>32 (50%)</td>
<td>25 (51.02%)</td>
<td>10 (66.66%) (n.s)</td>
</tr>
<tr>
<td>Mean age at first event</td>
<td>44.50</td>
<td>42.08</td>
<td>52.46 (p&lt;0.05)</td>
</tr>
<tr>
<td>Malignant disease*</td>
<td>5 (7.81%)</td>
<td>1 (2.04)</td>
<td>4 (26.66)</td>
</tr>
<tr>
<td>Other defects</td>
<td>5 (7.81%)</td>
<td>3 (6.12%)</td>
<td>2 (13.33%)</td>
</tr>
<tr>
<td>Oral contraceptives*</td>
<td>9 (14.06%)</td>
<td>7 (14.28%)</td>
<td>2 (13.33%)</td>
</tr>
</tbody>
</table>

HH: hyperhomocysteinemia; VTD: venous thromboembolic disease; *when cancer patients are excluded from the analysis, the patients with VTD show a tendency toward higher plasma homocysteine than control group (p=0.06); † only women considered, n.s.: non significant. Fisher’s exact test.
teinemia is considerably increased by using the latter test. After confirmation of the existence of hyperhomocysteinemia, other tests to study its possible origin (such as folate and vitamin B6 and B12, and investigation of renal function) as well as its treatment should be considered.

**Funding**

AC was supported by the Fundació per a la Bioquímica Clínica i Patologia Molecular.

**Key words**

Homocysteine, venous thrombosis, cardiovascular disease

---

**References**


---

**Scientific letters**

**Percutaneous umbilical blood sampling in the management of immune thrombocytopenic purpura during pregnancy**

Nicola Vanelle, Steffano Baravelli, Vincenzo Milano, Nicola Rizzo, Lucia Catani, Sante Tura

Severe neonatal thrombocytopenia occurs in about 15% of deliveries from women with immune thrombocytopenic purpura (ITP). Conflicting data exist about the real usefulness of percutaneous umbilical blood sampling (PUBS) in evaluating the fetal platelet count. We report successful experience, using PUBS, in the management of 12 pregnant women with ITP.

Immune thrombocytopenic purpura (ITP) is a common autoimmune disorder of young women, accounting for 3% of all cases of thrombocytopenia at the time of delivery. ITP in pregnancy can cause an impairment of maternal, fetal or neonatal hemostasis. A maternal platelet count of >30 × 10^9/L is only rarely associated with severe hemorrhage in pregnancy, during vaginal delivery or cesarean section. There is some debate as to the real risk to the fetus and neonate, regardless of maternal or fetal platelet count or the route of delivery.

Reported data show a 15% incidence of severe neonatal thrombocytopenia (platelet count <50 × 10^9/L), and a 1.5% incidence of intracranial hemorrhage (ICH). However, other authors have documented a lower incidence of severe neonatal thrombocytopenia without any hemorrhagic complications. Although some clinical and laboratory parameters have been proposed as being helpful in the identification of those pregnant women with ITP at risk of giving birth to severely thrombocytopenic neonates, conclusive data are lacking.

Sciscia et al. demonstrated the usefulness of percutaneous umbilical blood sampling (PUBS) in predicting fetal platelet count. PUBS may guide the mode of delivery and obviate unnecessary cesarean sections when fetal platelet count is ≥50 × 10^9/L. However, PUBS carries a risk of 1-2% of causing intrauterine fetal death or the need for urgent delivery.

Our experience concerns 12 pregnant women (median age 30 yrs, range 21-39 yrs) submitted to PUBS. None had hepatitis B, C or HIV. Seven patients had a previous diagnosis of chronic ITP, whereas the other 5 were diagnosed during pregnancy (median time of diagnosis 18th week, range 8th-31st week) according to McMillan’s criteria. Six patients were primigravida and 6 multipara, 3 of whom had previously delivered a thrombocytopenic neonate. Patients in whom PUBS showed a fetal platelet count <50 × 10^9/L were submitted to cesarean section. PUBS was most often performed during the 38th-39th week of pregnancy (Table 1) with a 20 gauge needle.

Fetal blood sampling was successfully achieved in all 12 patients without any complications. Three fetuses with a platelet count <50 × 10^9/L were delivered by cesarean section. Spontaneous vaginal delivery was allowed to occur in all the other cases. Fetal and neonatal platelet counts always correlated. The interval between PUBS and delivery ranged from 0-7