Turk J Hematol 2007; 24:90-92


LETTER TO THE EDITOR

# The prevalence of factor V Leiden (1691G-A) and methylenetetrahydrofolate reductase C677T mutations in healthy newborns in Bursa, Turkey

**Birol Baytan[1], Adalet Güneş Meral[1], Yesim Özarda İlçöl[2], Ünsal Günay[2]**

[1]Departmet of Pediatric Hematology Uludag University Faculty of Medicine, Bursa, Turkey
✉ *baytanbirol@yahoo.com*
[2]Departmet of Biochemistry Uludag University Faculty of Medicine, Bursa, Turkey

**Letter to the Editor**

The etiology of thromboembolism is thought to be multifactorial caused by congenital and acquired risk factors during childhood. Factor V G1691A or factor V Leiden (FVL) has been identified as the most common inherited risk factor [1,2]. Although the prothrombotic effect of methylenetetrahydrofolate reductase (MTHFR) C677T genotype is still debatable, it is also found to be responsible for causing thrombosis, particularly arterial, in different studies [3-5]. Previous studies carried out in Turkey showed an 8-10% prevalence of FVL [6-8] and 6-8% of MTHFR homozygosity [9,10]. However, it does not actually represent the whole country, which might show many ethnic differences, since Anatolia has been a crossroads for different races and ethnic groups throughout history, from Asia, Europe and Africa, resulting in a big variety in ethnicity. Bursa is a good example of such a city demonstrating this variety since it has a mixed population mostly of immigrants from the Balkans (Bulgaria, Greece and former Yugoslavia) who are ethnically Turkish. As there is no existing data in the different ethnic groups in Turkey, we aimed to study the prevalence of these two genetic disorders in healthy term newborns to show if there is any increased risk predisposing to thrombosis in Balkan immigrants.

Two hundred and fifty healthy term newborns (143 F/107 M) born at Zubeyde Hanım Maternity Hospital in Bursa were included in the study. No other conditions were required for inclusion besides being born at term and healthy. Informed written consent was obtained from each family. The ethnic background was queried. The neonates from the immigrant families from Bulgaria, Greece and former Yugoslavia were separately recorded.

The first group (Group I) consisted of the 250 neonates who were divided into two subgroups according to their ethnicity:

a. Group II: Neonates from Balkan immigrants (n:137).
b. Group III: Others excluding the immigrants (n:123).

Blood samples (2 ml) were collected into glass Vacutainer tubes containing EDTA (Becton Dickinson Vacutainer R Systems, Franklin Lakes, NJ) for DNA analysis. The buffy coat was separated from the supernatant plasma after 1800x g centrifugation for 10 minutes at room temperature. The buffy coats were kept at $4^0$C until DNA extraction within 24 hours. The genetic analyses for FV G1691A and MTHFR C677T polymorphism were performed with the aid of a commercial kit using real-time PCR thermocycler (Light Cycler, Roche, Germany).

Of the 250 newborns, 140 (56%) were found positive for the searched genetic disorders. The prevalence of FVL heterozygosity in the first group was found as 10.4% whereas it was 10.9% in Balkan immigrants (Group II) and 8% in Group III. When the prevalence of FVL heterozygosity was statistically compared, there was no significant difference between the second and third groups ($p>0.05$). The prevalence of homozygous and heterozygous states for MTHFR C677T polymorphism in the 250 neonates were 13.2% (n:33/250) and 32.4% (n:81/250), respectively. MTHFR heterozygosity in Balkan immigrants was found as 36.4% (n:50/137) whereas it was 25% (n:31/123) in the others; the rate was significantly higher in Balkan immigrants ($p<0.05$). However, the prevalence of homozygosity for the same polymorphism was found significantly higher in children with non-Balkan ethnic background (17.8% vs. 8%; $p<0.05$).

In the present study, the prevalence of FVL both in the general population and Balkan immigrants was found as approximately 10%. The data from previous studies in Turkey and the Balkans, such as Greece and Bulgaria, have also shown a similar prevalence, reporting it as around 10% [11-14]. We expected to find this similar frequency in our region considering that one-third of the population in Bursa migrated from the Balkans. The homozygous and heterozygous MTHFR C677T prevalence was found as 13% and 33%, respectively. Balta *et al.* [10] from Ankara, the capital located in the central part of Turkey, reported the same mutation as 6.3% for homozygous state and 27.8% for heterozygous. Our result is higher than this report. The difference could be explained by the regional variations in genetic background between these two provinces. This study has demonstrated that heterozygosity for this mutation was significantly frequent in the babies with Balkan ancestry whereas homozygosity was more frequent in the other group. However, the homozygous state for this mutation is reported as a risk factor for promoting thrombosis [3,15].

In conclusion, we found that children with Balkan ancestry do not have a higher incidence of FVL heterozygosity and MTHFR homozygosity compared to children with non-Balkan ethnicity. Therefore, they could be assumed as carrying low risk for thrombosis. This is useful information since a deeper knowledge about the regional variations in genetic backgrounds could facilitate better planning in taking public health decisions to prevent thrombosis in a country.

## References


1. Hagstrom JN, Walter J, Bluebond-Langner R, Amatniek JC, Manno CS, High KA. Prevalence of the factor V Leiden mutation in children and neonates with thromboembolic disease. J Pediatr 1998;133:777-81.
2. Andrew M, Monagle PT, Broker L. Thromboembolic complications during infancy and childhood. In: Andrew M, ed. Congenital Prothrombotic Disorders: Presentation During Infancy and Childhood. 1st ed. London: B.C. Decker Hamilton, 2000:51-102.
3. Brown K, Luddington R, Baglin T. Effect of the MTHFR C677T variant on risk of venous thromboembolism: interaction with factor V Leiden and prothrombin (F2G20210A) mutations. Br J Haematol 1998;103:42-4.
4. Balasa V, Gruppo RA. The relationship of mutation in the MTHFR, prothrombin and Pal-1 genes to the plasma level of homocysteine in children and adults. Thromb Haemost 1999;81:739-44.
5. Nowak-Göttle U, Strater R, Heinecke A, Junker R, Koch HG, Schuierer G, von Eckardstein A. Lipoprotein (a) and genetic polymorphism of clotting factor V, prothrombin and methylenetetrahydrofolate reductase are risk factors of ischaemic stroke in childhood. Blood 1999;94:3678-82.
6. Ozbek U, Tangün Y. Frequency of factor V Leiden in Turkey. Int J Hematol 1996;64:291-2.
7. Akar N, Akar E, Dalgın G. Frequency of factor V 1691 G-A in the Turkish population. Thromb Haemost 1997;39:313-5.
8. Gurgey A, Mesci L. The prevalence of factor V Leiden (1691 G-A) mutation in Turkey. Turk J Pediatr 1998;41:344-7.
9. Akar N, Akar E, Mısırlıoglu M, Avcu F, Yalçin A, Cin S. Search for genetic factors favoring thrombosis in Turkish population. Thromb Research 1998;79:79-82.
10. Balta G, Gurgey A. Methylenetetrahydrofolate reductase (MTHFR) 677 C-T mutation in Turkish patients with thrombosis. Turk J Pediatr 1999;41:197-9.
11. Akar N, Akar E, Dalgın G. Frequency of factor V 1691 G-A in the Turkish population. Thromb Haemost 1997;39:313-5.
12. Gurgey A, Mesci L. The prevalence of factor V Leiden (1691 G-A) mutation in Turkey. Turk J Pediatr 1998;41:344-7.
13. Chaida C, Gialeraki A, Tsoukala C, Mandalaki T. Prevalence of FVQ506 mutation in Hellenic population. Thromb Haeamost 1996;76:124-8.
14. Boyanovsky B, Russev M, Ganev V, Penev M, Baleva M. Prevalence of factor V Leiden and prothrombin 20210 A variant in Bulgarian patients with pulmonary thromboembolism and deep venous thrombosis. Blood Coagul Fibrinolysis 2001;12:639-42.
15. Ray JG, Shmorgun D, Chan WS. Common C677T polymorphism of the methylenetetrahydrofolate reductase gene and the risk of venous thromboembolism: meta-analysis of 31 studies. Pathophysiol Haemost Thromb 2002;32:51-8.