Factor V Leiden in Blood Donors in Baghdad (Iraq)

To the Editor:

Human coagulation factor V is a 330-kDa single-chain glycoprotein that plays an important role in the coagulation pathway. After its activation by thrombin and factor Xa, activated factor V (Va) forms an essential part of the prothrombinase complex, which catalyzes the conversion of prothrombin to thrombin in the presence of calcium and a phospholipid membrane (1). Activated protein C (APC) inactivates factor Va and requires factor V as a cofactor in the APC-mediated inactivation of factor V (1, 2). Resistance to APC action leads to increased risk of thrombosis and is mostly attributable to a single point mutation in the factor V gene (factor V Leiden) with a G-to-A substitution at nucleotide 1691 (3).

Several studies have demonstrated the high prevalence of factor V Leiden in some Middle Eastern countries, with suggestions that the eastern Mediterranean basin maybe the site where this mutation arose ~21 000–34 000 years ago (4, 5). Despite the fact that Iraq lies within this region, no such prevalence studies have been reported on the incidence of factor V Leiden in that country. We report here the results of the first such study.

Between September 21, 2002, and February 22, 2003, we evaluated a total of 100 blood donors attending the national blood bank, the only blood-banking facility serving the population of Baghdad City and the surrounding regions in central Iraq. Samples were collected, through venipunctures separate from those used for donation, from 10 donors randomly selected by use of random numbers (between 1 and 40, generated for each day) from among the first 40 attending the bank on 10 alternate Saturdays throughout the study. During the first nine collection sessions, one randomly selected donor declined participation, and one sample was hemolyzed; therefore, on the last session, 12 random samples were taken. The study was approved by the Council of the College of Medicine-University of Baghdad, and informed consent was obtained from all donors evaluated.

All included patients were males, consistent with the donation pattern in Iraq, with ages ranging from 18 to 52 years (median, 30.5 years). A second-generation APC resistance test was performed on all included patients with a STAACL® APC-R reagent set (Diagnostica Stago) with modifications; 100 μL of prediluted test plasma (1:10 in factor V-deficient plasma) was incubated for exactly 3 min at 37°C with 100 μL of Crotalus viridis helleri venom, after which 100 μL of APC/calcium chloride was added, and the clotting time was recorded. The clotting times ranged from 39 to 111 s, with a mean (SD) of 70.4 (13.5) s. The cutoff point for “resistant” cases was 48 s as determined by logarithmic transformation of clotting times, after exclusion of outliers (<3 SD above or below the mean) and calculation of the mean – 1.96 SD. All included donors had their DNA extracted, amplified, hybridized to wild- and mutant-type DNA probes, and detected by enzyme immunoassay according to the instructions of the manufacturer (ViennaLab). Four cases (4%) were below the calculated cutoff point of the second-generation APC test and were thus considered resistant. Three cases (3%) were found to be heterozygous for factor V Leiden by DNA studies (all of whom were APC resistant with clotting times of 43, 45, and 48 s). The remaining case, resistant by second-generation APC resistance tests (clotting time, 39 s) was a non-carrier of factor V Leiden. This may indicate that an alternative mutation involving the factor V gene maybe responsible for APC resistance in this particular case (6).

The prevalence rate of 3% in Iraqi blood donors, although it is much lower than the prevalence rates of 14.2%, 13.6%, and 12.25% reported in Lebanon, Syria, and Jordan, respectively (4, 7), and to a lesser extent than the rates in Turkey (7.4%) (8) and Iran (5.5%) (9), is comparable to the prevalence of 2.5% reported in

References


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DOI: 10.1373/clinchem.2003.029512
Saudi Arabia (10). The latter may be related to a common origin and closer links between the population of Iraq (including Baghdad) and that of the Arabian Peninsula throughout history.

References

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DOI: 10.1373/clinchem.2003.029314

To the Editor:

Taieb et al. (1) in their recent report in Clinical Chemistry described the relationship of serum testosterone concentrations measured by 10 immunoassays and by isotope-dilution gas chromatography–mass spectrometry (ID/GC-MS). Automated immunoassays fared badly, but RIAs agreed well with the ID/GC-MS.

In contrast to our findings, Taieb et al. (1) reported, in women, increased serum testosterone as assayed in the AutoDelfia immunoassay system (Perkin-Elmer). Between November 1, 2002, and February 28, 2003, we found for 2057 women a mean (median) testosterone of 2.1 (1.6) nmol/L by AutoDelfia, similar to the values of 1.7 (1.4) nmol/L for 2180 different female samples assayed consecutively in our routine using the Orion Diagnostica RIA between November 1, 2001, and February 28, 2002. By contrast, Taieb et al. (1) reported mean concentrations of ~5 nmol/L in the female samples measured by the AutoDelfia.

In the same time periods, consecutively male samples had mean (median) values of 16.7 (14.8) nmol/L by AutoDelfia (n = 1447) and 13.9 (12.9) nmol/L by the Orion (n = 1505). Again, the difference between the automated immunoassay and RIA values was much smaller than reported by Taieb et al. (1).

In our hands the main difference between the automated immunoassay and the RIA for the determination of testosterone in female samples was a much higher frequency of increased concentrations in individual samples caused by interfering substances in the AutoDelfia. This led us to resume use of the RIA. Although interference in RIAs for testosterone does happen (2), interferences appeared to be less frequent than in the automated immunoassay systems we have tested. It would be of great interest if Taieb et al. (1) could report the rate of interference leading to increased concentrations in individual samples in the different immunoassay methods they used in their study with ID/GC-MS as the reference.

References

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DOI: 10.1373/clinchem.2003.027565

To the Editor:

Torjesen and Sandnes briefly summarize our study (1) that compared testosterone immunoassays with an isotope-dilution gas chromatography–mass spectrometry (ID/GC-MS) method. They report mean concentrations in female samples lower than ours for the AutoDelfia system and describe two indirect personal observations to explain our 2.5-fold higher values: One is a very rare IgG that reacted with the labeled antibody of a direct isotopic assay from Orion Diagnostica (2), and the other concerned “a much higher frequency of increased concentrations in individual samples caused by interfering substances in the AutoDelfia.” It should be stated that before being assayed, all of our samples were selected in a blind manner with respect to previously described criteria (1). These samples were not problematic in immunoassays but were evaluated because they corresponded to our daily recruitment.