cations due to iron overload and on desferrioxamine therapy was not increased among those with TFR2 polymorphisms. Our results show that the TFR2 polymorphisms, I238M and IVS16 +251 CA deletion, while prevalent in Chinese patients, do not influence the degree of iron loading in transfusion-independent β-thalassemia intermedia. These TFR2 polymorphisms are therefore not useful in explaining the severe iron overload that may be encountered in our patients. This agrees with findings on I238M polymorphism in normal Asian subjects. Furthermore, detection of common HFE polymorphisms is also not expected to be fruitful, given the low prevalence of these in our area. Nevertheless, the presence of other, hitherto-unknown genetic determinant(s) of iron overload in the Chinese population cannot be excluded and may need to be unraveled in the future.

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Key words: TFR2 polymorphism, iron overload, β-thalassemia intermedia, genetic hemochromatosis.

Manuscript processing

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References


Molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Fars province of Iran

We investigated 78 glucose-6-phosphate dehydrogenase (G6PD)-deficient alleles from the Fars province of Iran by polymerase chain reaction–single strand conformation polymorphism (PCR-SSCP) and direct sequencing. The frequency of G6PD Mediterranean in Fars was 84.6%, G6PD Chatham was found to be highly polymorphic and two other sporadic variants (G6PD A– and G6PD Canton) were detected in single cases.

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme disorder in humans and is characterized by considerable biochemical and molecular heterogeneity. The prevalence of G6PD deficiency in the Middle East varies greatly, ranging from 1% among Egyptians to 11.55% among Iranians. G6PD Mediterranean (563 C→T) mutation is probably the most common G6PD variant in the world; it has been widely reported in Europe but also in the Middle-East and in neighboring countries not bordering the Mediterranean sea. Among the known variants, the relative frequency of this mutation ranges from 70% among Egyptians to 97% for Kurdish Jews. A recent study carried out on the population of the Mazandaran state of North Iran near the Caspian sea showed a frequency for the G6PD Mediterranean mutation of 66.2% and the presence of two other polymorphic mutations: G6PD Chatham and G6PD Cosenza. We report here a study performed on 78 G6PD-deficient alleles from a different population of Iran, originating from the Fars province, located in the South of the country. The incidence of G6PD deficiency in this area is estimated to be about 12% in males and 0.9% in females. The study was carried out on 74 unrelated G6PD deficient subjects (66 males, 8 females) aged between 10 days to 20 years (mean 8.5 years) all originating from the Fars province of Iran. The subjects were recruited from neonatal and school screening. The diagnosis of G6PD deficiency was based on the fluorescent spot test. Clinical data were recorded considering neonatal jaundice, favism or drug-related hemolysis.

As preliminary screening, the following polymorphic G6PD molecular variants were tested by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP): G6PD Mediterranean, G6PD A–, and G6PD Canton. The G6PD Mediterranean mutation was detected in 62/74 (83.8%) samples. Four females were homozygous for this mutation, leading to an overall allele frequency of 84.6%. Among the other variants screened for, we identified one subject with G6PD A– (1.3%) whereas G6PD Canton, G6PD Seattle, and G6PD A– were absent from all our samples. The 11 negative samples were submitted to SSCP analysis of the entire G6PD coding region that allowed us to identify two different abnormal patterns in exon 9 and 12, respectively. Nucleotide sequencing of exon 9 revealed a G to A substitution at nt 1003 responsible for...
be different. In fact, G6PD Cosenza, identified for the first time in Italy, is a known variant already described in the Middle-East and in the Mediterranean probably migrating from Western countries to Iran. By contrast, G6PD Canton is one of the most common variants in the South East of Asia and is likely to have been spread during the agricultural migration from China.

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Key words: G6PD deficiency, G6PD mutations, Iran, molecular characterization.

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**References**

**Table 1. Frequencies of G6PD mutations in the Fars province of Iran.**

<table>
<thead>
<tr>
<th>Molecular variant</th>
<th>Cases</th>
<th>(%)</th>
<th>Alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediterranean (563 C→T)</td>
<td>62</td>
<td>83.78</td>
<td>66</td>
</tr>
<tr>
<td>Chatham (1003 G→A)</td>
<td>10</td>
<td>13.51</td>
<td>10</td>
</tr>
<tr>
<td>A- (202 G→A/376 A→G)</td>
<td>1</td>
<td>1.35</td>
<td>1</td>
</tr>
<tr>
<td>Canton (1376 G→T)</td>
<td>1</td>
<td>1.35</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>100</td>
<td>78</td>
</tr>
</tbody>
</table>

**Table 2. Clinical data of the 74 G6PD-deficient subjects.**

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>Total</th>
<th>Med</th>
<th>Chatham</th>
<th>A-</th>
<th>Canton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic anemia</td>
<td>35</td>
<td>29/35</td>
<td>5/35</td>
<td>1/35</td>
<td>0/35</td>
</tr>
<tr>
<td>Neonatal jaundice</td>
<td>24</td>
<td>18/24</td>
<td>5/24</td>
<td>0/24</td>
<td>1/24</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>41</td>
<td>35/41</td>
<td>5/41</td>
<td>1/41</td>
<td>0/41</td>
</tr>
</tbody>
</table>