Transferrin C Subtypes in Saudi Arabia: A Study in the Central Province

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In this study the frequency of transferrin (TF) C subtypes was investigated in 150 individuals from the central province of Saudi Arabia. The frequencies of the TF C1, C2, C3 and D genes were 0.6934, 0.2467, 0.0433 and 0.0167, respectively.

Transferrin is in the β-globulin fraction of serum proteins. It specifically binds two atoms of free iron to each molecule and serves to transport iron from the sites of haemoglobin breakdown and intestinal absorption to the sites of utilization and iron storage. Like several other plasma proteins transferrin exhibits a genetically controlled polymorphism, and is considered a useful genetic marker.¹ More recently an isoelectric focusing technique has been shown to be very successful in separating the transferrin phenotypes.² Several population studies have been carried out to determine the frequency of transferrin (TF) phenotypes, and over 20 different variants have been reported using electrophoresis and isoelectric focusing.³⁻⁵ Furthermore, some studies have reported a significant association between the phenotype TF C2 and rheumatoid arthritis,⁶ photodermatosis,⁷ spontaneous abortion⁸ and prematurity.⁹

We conducted this pilot study in order to investigate the transferrin polymorphism among Saudis. In this paper we present our findings and compare the results with those reported in literature for other populations.

Materials and Methods

The subjects investigated were all Saudis from the central province of Saudi Arabia (Riyadh). A total of 150 blood samples were collected from healthy individuals. The plasma was separated from the red cells by centrifugation and stored frozen at −20°C until required for analysis.

Prior to isoelectric focusing the plasma sample was prepared according to the procedure given in LKB (Bromma) Application Note No. 473. For isoelectric focusing, ‘Immobile Dry Plates’, pH range 5.0–6.0 (LKB Cat No. 1824, LKB–Produkter AB, Bromma, Sweden) were rewelled for 2 h and prefocussed at 2000 V, 4.0 mA, 12 W at 10°C for 30 min using LKB 2117 Multiphor II. After sample application, isoelectric focusing was carried out for 3 h at 10°C by applying 2000 V, 4.0 mA and 12 W. The gel was fixed, stained and destained according to the procedure provided in the LKB instruction No. 472.

Results

The transferrin phenotypes, TF C1, C2, C3, C1C2, C1C3, C2C3, C1D and C2D, were identified on isoelectric focusing in an immobile pH gradient (Table 1). Five samples had TFD in association with transferrin C subtypes, TFC1 or C2 at a prevalence of 2.67% and 0.67%, respectively. Observed values were in good agreement with Hardy Weinberg expectations in most cases, except the observed value for TFC3 was significantly more than the expected value.

The gene frequencies of TF C1, C2, C3 & D are presented in Table 2. The most common TF C subtype in Saudis was TF C1 followed by TF C2.
Table 1
Prevalence of transferrin phenotypes in the Saudi Population

<table>
<thead>
<tr>
<th>Transferrin phenotypes</th>
<th>Observed no.</th>
<th>Expected no.</th>
<th>Value of $\chi^2$</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>73</td>
<td>72.04</td>
<td>0.0127</td>
<td>0.4867</td>
</tr>
<tr>
<td>C2</td>
<td>9</td>
<td>9.13</td>
<td>0.0024</td>
<td>0.0600</td>
</tr>
<tr>
<td>C3</td>
<td>2</td>
<td>0.28</td>
<td>10.565*</td>
<td>0.0133</td>
</tr>
<tr>
<td>C1C2</td>
<td>52</td>
<td>51.32</td>
<td>0.0082</td>
<td>0.3467</td>
</tr>
<tr>
<td>C1C3</td>
<td>6</td>
<td>9.01</td>
<td>0.9668</td>
<td>0.0400</td>
</tr>
<tr>
<td>C2C3</td>
<td>3</td>
<td>3.20</td>
<td>0.0113</td>
<td>0.0200</td>
</tr>
<tr>
<td>C1D</td>
<td>4</td>
<td>3.47</td>
<td>0.0626</td>
<td>0.0267</td>
</tr>
<tr>
<td>C2D</td>
<td>1</td>
<td>1.24</td>
<td>0.0536</td>
<td>0.0067</td>
</tr>
<tr>
<td>Total</td>
<td>150</td>
<td>149.77</td>
<td>11.683**</td>
<td>1.0001</td>
</tr>
</tbody>
</table>

*Significant.
**df = 7.0 non-significant.

Table 2
Transferrin genotype frequencies with SE

<table>
<thead>
<tr>
<th>Transferrin genotype</th>
<th>Gene frequencies with SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFC1</td>
<td>0.6934 ± 0.0266</td>
</tr>
<tr>
<td>TFC2</td>
<td>0.2467 ± 0.0288</td>
</tr>
<tr>
<td>TFC3</td>
<td>0.0433 ± 0.0117</td>
</tr>
<tr>
<td>TFD</td>
<td>0.0167 ± 0.0074</td>
</tr>
</tbody>
</table>

Discussion
This study showed transferrin polymorphism among the Saudi population in the central province of the country. The major transferrin was transferrin C which occurred at a gene frequency of 0.9834 and the TFC subtypes i.e. TFC1, TFC2 and TFC3 were identified. The most common transferrin C subtype in Saudis was TF C1 which occurred at a gene frequency of 0.6934. TF C1 is reported as the most common transferrin variant in studies so far reported on Chinese, Japanese, Indonesians, Indians, Polynesians, Fijians, Australians, Black Americans, White Americans and Jordanians, though its frequency varies significantly from 0.47 to 0.91 in different populations. The highest frequency is encountered in the Micronesians and the lowest in Fiji Indians. In the Saudi population the gene frequency of C1 was similar to that reported for Asiatic Indians.

TF C2 was identified both in homozygous and heterozygous states. The gene frequency of TF C2 was 0.2467 in the Saudi population. This frequency was higher than that reported for most of the populations, but similar to that reported for Asiatic Indians and Bedouin and non-Bedouin Jordanians. The TF C2 occurs at a frequency ranging from 0.05 to 0.26 in different populations. The lowest frequency is reported in Africans and the highest is reported in the Japanese.

The association of TF C2 with photoallergic eczema (photodermatosis), rheumatoid arthritis, high incidence of spontaneous abortion and increased risk of prematurity has been shown in several studies.5-9,14 Among populations such as Saudi Arabia where TF C2 occurs at a high prevalence further detailed investigations are necessary to confirm this association, and to investigate other associated clinical consequences.

Transferrin C3 was also identified both in homozygous and heterozygous states, however, the observed frequency of phenotype TFC3 was significantly higher than the expected frequency. It was earlier considered by Kamboh & Kirk11 as a specific marker for European (Caucasians) populations. However, later it was reported in American Whites and in Asiatic Indians.5 Our study also revealed that TF C3 occurs in the Saudi population in the central region of Saudi Arabia. Kamboh & Ferrell5 in their excellent review on transferrin suggest that TF C3 might have first arisen due to mutation in the European populations and subsequently due to recent admixture, became introduced in other populations.

The TF D was identified only as heterozygotes at a gene frequency of 0.0167 in the Saudis. In Jordanians, Saha10 reported a gene frequency of 0.006. In most populations a low gene frequency for TF D has been reported.

In conclusion, the results of this pilot study show that transferrin exhibits polymorphism in Saudis and the frequency of the polymorphic forms in the population of central province of Saudi Arabia, is similar to that reported in Caucasians, Jordanians and Indians. However, further studies are essential to identify rare transferrin variants, to determine the frequency of transferrin variants in different provinces of Saudi Arabia since regional differences are reported within different countries, and to investigate the possible associations between transferrin phenotypes and disease states.

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References


