identified in this gene, SNPs (12, 13) remain the only available genetic markers for linkage analysis to identify presymptomatic carriers in AIP families.

We thank S.F. Tong for technical support.

References


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Reference Values of Serum IgA Subclasses in Caucasian Adults by Immunonephelometry

To the Editor:

Immunoglobulin A (IgA) is a glycoprotein present in plasma (as part of the systemic compartment) and in body secretions (as part of the secretory compartment). Two different subclasses, IgA1 and IgA2, have been described. The IgA1/IgA2 ratio is much higher in the systemic compartment than in the secretory compartment. Serum IgA2 concentrations have been used as an index for mucosal pathology (1, 2). Changes in serum IgA subclass concentrations and changes of the IgA1/IgA2 ratio have been associated with specific diseases and conditions, e.g., subclass deficiency leading to anaphylactic transfusion reactions, chronic alcohol abuse (increased IgA2 concentration and IgA2/IgA1 ratio) (3), and primary IgA nephropathy (increased IgA1 in Caucasians) (4).

Various methods (e.g., immunoradiometry, immunodiffusion, and ELISA) that use subclass-specific antisera (2) or monoclonal antibodies (4–6) have been proposed for the determination of IgA subclass concentrations in various human body fluids. Recently, subclass-specific antisera have been introduced for application in a nephelometric assay.

The aim of our study was to establish reference values for serum concentrations of the two IgA subclasses in Caucasian adults, using this immunonephelometric assay.

Total IgA and IgA subclasses were assayed using commercial reagents (Hu IgA Subclass BNA Kit; The Binding Site, Birmingham, UK) on a Behring nephelometer (Behringwerke AG). The coefficient of variation, calculated from the results of 10 consecutive determinations of a single sample, was 2.6% for total IgA (at a mean concentration of 1.02 g/L), 4.3% for IgA1 (at a mean concentration of 1.12 g/L), and 3.6% for IgA2 (at a mean concentration of 0.11 g/L). The total serum IgA concentration was standardized against the IFCC/BCR/CAP Reference Material (CRM 470) (7).
The reference subjects were examined by a physician. A questionnaire was used to eliminate recent illnesses, pregnancy, and alcohol (>25 g daily) or drug abuse. Subjects suffering from cardiovascular, endocrine, rheumatic, hematological, infectious, or genito-urinary diseases were excluded from the study. Serum samples were obtained by venipuncture from 276 healthy Belgian individuals. Two samples with a selective IgA2 deficiency were collected and were excluded from the study. For determination of reference intervals, we included 274 serum samples from 124 women and 150 men between 18 and 65 years of age.

The serum concentrations, given as the median and interquartile range, of total IgA, IgA1, and IgA2 according to sex and age are shown in Table 1. The minimum of 120 subjects needed to determine reference values reliably was achieved in the two sex groups, but not in the different individual age groups (8).

Serum concentrations of total IgA were higher in men (median, 2.08 g/L; range, 1.49–2.68 g/L) than in women (median, 1.69 g/L; range, 1.24–2.17 g/L; P < 0.001), which is in agreement with previous observations (7). This finding was also observed for the serum concentrations of the two IgA subclasses, with men showing significantly higher concentrations than women: for IgA1, 1.80 g/L (1.26–2.35 g/L) for men vs 1.50 g/L (1.03–1.91 g/L) for women (P < 0.001); and for IgA2, 0.43 g/L (0.28–0.61 g/L) for men vs 0.33 g/L (0.24–0.47 g/L) for women (P < 0.001). The between-gender statistical difference was further evaluated by a standard normal deviate test (z-test): the critical z value (z*) was 3.21, and the calculated z values were 3.78 for total IgA, 3.65 for IgA1, and 4.67 for IgA2 (8). The IgA1/IgA2 ratio was not statistically different between genders: 4.44 ± 1.81 for men vs 4.81 ± 1.85 for women; P = 0.07.

The 95% central intervals, which presently are used for interpretive and diagnostic purposes, were 0.72–3.89 g/L for total IgA, 0.61–3.79 g/L for IgA1, and 0.12–1.17 g/L for IgA2 in the male population, and 0.73–3.39 g/L for total IgA, 0.61–3.19 g/L for IgA1, and 0.09–0.69 g/L for IgA2 in the female population.

We found a positive correlation between serum IgA2 and the age of the subjects: y (serum IgA2, mg/L) = 6.71x (age, years) + 151.12; r = 0.340; n = 274; S_{yx} = 224.54; P < 0.001. Table 1 shows the data in different age groups. The IgA1/IgA2 ratio was found to be lower in the older population: 4.20 ± 1.59 (>40 years, n = 150) vs 5.10 ± 1.99 (≤40 years, n = 124); P < 0.001.

The sum of the IgA subclasses was slightly higher than the total IgA concentration: the (IgA1 + IgA2)/total IgA ratio was 1.09 ± 0.12.

In conclusion, we have established gender-related reference intervals for IgA1 and IgA2 in serum from human adults, using immunonephelometry. When evaluating IgA1 and IgA2 serum concentrations, one should take into account the patient’s age and gender for correct interpretation.

We thank The Binding Site (Birmingham, UK) for providing the reagents to perform this study.

Table 1. Serum concentrations* of total IgA, IgA1, and IgA2 according to age and gender.

<table>
<thead>
<tr>
<th>Age, years</th>
<th>n</th>
<th>Total IgA, g/L</th>
<th>IgA1, g/L</th>
<th>IgA2, g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–30</td>
<td>34</td>
<td>2.11 (1.36–2.58)</td>
<td>1.86 (1.26–2.35)</td>
<td>0.30 (0.22–0.43)</td>
</tr>
<tr>
<td>31–40</td>
<td>47</td>
<td>1.91 (1.32–2.52)</td>
<td>1.66 (1.17–2.17)</td>
<td>0.46 (0.29–0.68)</td>
</tr>
<tr>
<td>51–65</td>
<td>41</td>
<td>2.36 (1.57–2.98)</td>
<td>1.88 (1.36–2.49)</td>
<td>0.54 (0.36–0.67)</td>
</tr>
<tr>
<td>Total</td>
<td>150</td>
<td>2.08 (1.49–2.68)</td>
<td>1.80 (1.26–2.35)</td>
<td>0.43 (0.28–0.61)</td>
</tr>
</tbody>
</table>

References

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