Reference values for serum creatinine concentrations with Jaffe-compensated assay in Iranian adult subjects

Asghar Ghasemi, Iraj Azimzadeh, Saleh Zahediasl, Fereidoun Azizi

Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Introduction

Chronic kidney disease is a worldwide public health problem with increasing prevalence and incidence.

Glomerular filtration rate (GFR), the best overall index of renal function, is mostly estimated from serum creatinine concentration.

Any equation using serum creatinine level for estimating GFR is dependent on the serum creatinine assay.

Hetu PO: Clin Biochem 43:1158-1162, 2010

Dr. Ghasemi
Introduction

Serum creatinine concentration is affected by factors other than creatinine filtration including:

- Sex
- Age
- Race
- Diet
- Muscle mass
- Analytical method


Dr. Ghasemi
Jaffe method, used in most routine laboratories, has a low specificity and overestimates serum creatinine by approximately 20-30% at physiological values, because of noncreatinine chromogens (mainly proteins).

Enzymatic creatinine methods are more specific and have been widely adopted for routine clinical laboratory as alternatives to the alkaline picrate methods.
Introduction

For serum creatinine, like other naturally occurring biochemical compounds, a reference interval needs to be provided.

Reports of reference intervals for serum creatinine levels in Asian populations, considering IFCC (International Federation of Clinical Chemistry) criteria with accurate description of the measurement method, are scant.

To our knowledge, there is no documented report on reference values of serum creatinine in Iran.


Dr. Ghasemi
Aim

To determine age- and sex-specific reference intervals for serum creatinine concentration using data from a population-based study from Iran
Subjects and Methods

Subjects

Participants of Tehran Lipid and Glucose Study (TLGS) from June 2008 to September 2011

Number of subjects

5247 apparently healthy participants (2792 men and 2455 women), aged 20 to 88 years

Separate analysis was done for healthy menopausal women (n= 452; age range 51-84 years).
Subjects and Methods

Exclusion criteria

- Pregnancy
- Hypertension
- Diabetes
- History of cardiovascular disease, cancer, and diarrhea
- History of hospitalization during the past 3 months
- History of significant weight loss during past 6 months
- Using medications including steroids, diuretics, betablockers, digitalis, calcium channel blockers, angiotensin converting enzyme inhibitors, aspirin and other anticoagulants, lipid lowering drugs, male or female hormones, contraceptives (oral or injection), or drugs for thyroid disorders.
Creatinine measurement

Serum creatinine was measured using the photometric Jaffe method (Pars Azmoon Kit, Tehran, Iran)

In 382 samples, creatinine measurement was done with both Jaffe and enzymatic p-aminophenazone (PAP) methods

Method for determining reference values:

IFCC criteria (non-parametric method)
Results
Regression line between Cr measurement with Jaffe and PAP (enzymatic) methods

\[ \text{Jaffe Cr} = 0.863 \times \text{PAP Cr} + 0.44 \text{ mg/dL} \]

\[ r = 0.973, n= 383, p < 0.001 \]
Bland-Altman method comparison for comparing creatinine measurements by Jaffe and PAP methods

\[ \text{Mean} = 0.32 \pm 0.05 \]

\[ +2\text{SD} = 0.42 \]

\[ -2\text{SD} = 0.22 \]
Comparison of serum creatinine concentration according to sex and age

*: significant difference with other groups
†: significant difference compared to men

Dr. Ghasemi
Reference intervals for serum creatinine concentration (mg/dL) in healthy adult subjects according to age and sex using the compensated Jaffe method

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>n</th>
<th>95% Reference intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>856</td>
<td>0.53-1.00</td>
</tr>
<tr>
<td>30-39</td>
<td>633</td>
<td>0.53-1.00</td>
</tr>
<tr>
<td>40-50</td>
<td>701</td>
<td>0.53-1.11</td>
</tr>
<tr>
<td>&gt;50</td>
<td>602</td>
<td>0.53-1.11</td>
</tr>
<tr>
<td>All</td>
<td>2792</td>
<td>0.53-1.11</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>972</td>
<td>0.31-1.77</td>
</tr>
<tr>
<td>30-39</td>
<td>818</td>
<td>0.42-0.77</td>
</tr>
<tr>
<td>40-50</td>
<td>665</td>
<td>0.42-0.77</td>
</tr>
<tr>
<td>&gt;50</td>
<td>452</td>
<td>0.42-0.88</td>
</tr>
<tr>
<td>All</td>
<td>2455</td>
<td>0.42-0.77</td>
</tr>
</tbody>
</table>
Discussion
Serum creatinine reference values (mg/dL) in selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Age (years)</th>
<th>Creatinine reference values (μmol/L)</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Australia (Adelaide)</td>
<td>2000</td>
<td>18-70</td>
<td>Males 0.70-1.20 Females 0.50-0.91</td>
<td>Compensated Jaffe</td>
</tr>
<tr>
<td>Germany</td>
<td>2004</td>
<td>18-74</td>
<td>Males 0.71-1.17 Females 0.54-0.96</td>
<td>Compensated Jaffe</td>
</tr>
<tr>
<td>Nordic countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Denmark, Finland, Iceland,</td>
<td>2004</td>
<td>≥18</td>
<td>Males 0.70-1.20 Females 0.63-1.00</td>
<td>Compensated Jaffe</td>
</tr>
<tr>
<td>Norway, and Sweden)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>2006</td>
<td>20-60</td>
<td>Males 0.80-1.30 Females 0.60-1.00</td>
<td>Enzymatic</td>
</tr>
<tr>
<td>Spain</td>
<td>2007</td>
<td>19-65</td>
<td>Males 0.72-1.20 Females 0.59-0.96</td>
<td>Compensated Jaffe</td>
</tr>
<tr>
<td>Belgium</td>
<td>2008</td>
<td>20-70</td>
<td>Males 0.63-1.17 Females 0.48-0.93</td>
<td>Enzymatic</td>
</tr>
<tr>
<td>Italy</td>
<td>2010</td>
<td>18-79</td>
<td>Males 0.65-1.17 Females 0.45-1.00</td>
<td>Compensated Jaffe</td>
</tr>
<tr>
<td>China</td>
<td>2011</td>
<td>20-91</td>
<td>Males 0.66-1.11 Females 0.49-0.79</td>
<td>Enzymatic</td>
</tr>
<tr>
<td>Kenya</td>
<td>2012</td>
<td>18-50</td>
<td>Males 0.63-1.12 Females 0.54-0.96</td>
<td>ND</td>
</tr>
<tr>
<td>Iran</td>
<td>Present</td>
<td>20-88</td>
<td>Males 0.53-1.11 Females 0.42-0.77</td>
<td>Compensated</td>
</tr>
</tbody>
</table>
Conclusion

1. Reference intervals for serum creatinine concentration according to compensated Jaffe method, derived from a population-based study in Iran, are 0.53-1.11 and 0.42-0.77 mg/dL in men and women respectively.

2. Upper limits of serum creatinine reference values are lower than European countries and are close to the China and Kenya.

3. These values could be used for research, diagnostic and therapeutic purposes.
Thanks
Intra-assay CVs were 2.2% and 3.1% for Jaffe and PAP method respectively (n=72).

Inter-assay CVs for normal creatinine concentration were 4.1% and 6.1% for Jaffe and PAP method respectively and for high creatinine concentration were 1.3% and 1.7% for Jaffe and PAP method respectively (n=17).