A laboratory harmonization strategy for steroid hormone profiling by MoM-transformed, normalized reference ranges independent of age-, sex- and units

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Conclusion:
Age- and sex-independent MoMs are straightforward for clinically relevant display of multisteroid patterns. In addition, defined single steroid MoMs can serve alone as predictors for 21OHD and 11OHD. Finally, MoM-transformation offers a valuable strategy of national and international routine - and scientific steroid hormone data exchange due to improved comparability.

Introduction:
The high complexity of Pediatric reference ranges across age, sex and units impairs clinical application and comparability of steroid hormone data, e.g., in CAHs. We developed a Multiples-of-Median (MoM) normalization tool to overcome this major drawback in Pediatric Endocrinology.

Method and Subjects:
Multiples of Median MoM-calculation: Hormone concentrations in a given patient are divided through the median of the age- and sex-specific reference range. LC-MS/MS data comprising 10 steroid hormones representing 905 controls (555 males, 350 females, 0 to >16 years) from two previous datasets were MoM-transformed across age and sex. 24 genetically proven CAH patients were included (21OHD, N=19; 11OHD, N=5). As example, two different patients with 21OHD are chosen:

Patient 1: female, age: 3.9 years, presumend diagnosis: bone age acceleration

Patient 2: male, age: 10 days presumend diagnosis: 21OHD because of elevated 17OHP in newborn screening

Results:
21OHD and 11OHD showed disease-typical MoM-patterns across the 10-steroid LC-MS/MS profile, Figure 5. In addition, MoM-cut-offs for single steroids were computed for predicting 21OHD and 11OHD, respectively, Table 2.

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Patient 1</td>
<td>Patient 2</td>
</tr>
<tr>
<td>N 1978</td>
<td>0.035</td>
<td>0.035</td>
</tr>
<tr>
<td>Male 218</td>
<td>0.035</td>
<td>0.035</td>
</tr>
<tr>
<td>110HD cut-off</td>
<td>0.035</td>
<td>0.035</td>
</tr>
<tr>
<td>11S 100%</td>
<td>0.035</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Table 1: Reference ranges of 17-Hydroxy-Progesterone, 17OHP, for female and males, aged 0-18 years.

Table 2: Single steroid cut-off MoMs

The single cut-off values were validated through new, independent patients, Figure 6.

- 21OHD, N=8
- adrenal cortical carcinoma, N=6
- obesity, N=40

References:

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Adrenals and HPA axis: RFC1.6