Quality of Factor XI Activity Testing in North American Specialized Coagulation Laboratories

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BACKGROUND

- Factor XI (FXI) plays a role in initiation and propagation of coagulation.
- Congenital factor XI deficiency is a rare autosomal bleeding disorder, but is observed at higher rates among Ashkenazi Jews.
- FXI is not usually associated with spontaneous bleeding, but is associated with a bleeding risk with hemostatic challenges particularly in areas with high levels of fibrinolysis.
- High levels of FXI level have been associated with thrombosis.
- Accurate measurement of FXI is important for diagnosis and treatment.

METHODS

- The performance of factor XI by North American Specialized Coagulation Laboratory Association (NASCOLA) laboratories in the External Quality Control of Diagnostic Assays and Tests (ECAT) foundation proficiency testing program was analyzed for 2008-2012.
- 20 surveys were performed with 40 specimens (34 specimens tested once and 3 specimens tested twice).
- Participants classified their results as normal, borderline normal, borderline abnormal, or abnormal.

RESULTS

Classification of Results

<table>
<thead>
<tr>
<th>Factor XI Activity (IU/dL)</th>
<th>Normal</th>
<th>Borderline Normal</th>
<th>Borderline Abnormal</th>
<th>Abnormal</th>
<th>No Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
<td>100 (97%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>40-&lt;50</td>
<td>18 (3%)</td>
<td>15 (10%)</td>
<td>46 (10%)</td>
<td>384 (82%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>50-&lt;80</td>
<td>148 (5%)</td>
<td>11 (5%)</td>
<td>13 (6%)</td>
<td>37 (18%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>≥80</td>
<td>1241 (96%)</td>
<td>5 (0.4%)</td>
<td>13 (1%)</td>
<td>25 (2%)</td>
<td>13 (1%)</td>
</tr>
</tbody>
</table>

- Two samples with FXI levels < 40 IU/dL were correctly classified as normal or borderline abnormal by 99% (101/102) of participants.
- Specimens with FXI ≥ 80 IU/dL were classified as normal or borderline normal by 97% (1247/1284) of participants.
- The classification of samples with high results was mixed as to whether laboratories reported values as normal or abnormal.
- Result classification as abnormal or normal was heterogeneous in specimens with FXI levels between 40 IU/dL and 80 IU/dL.

Intra-Laboratory Precision

- 3 specimens tested on 2 surveys
- Results were compared from laboratories using the same method on both surveys.
- Average FXI result for the first test was 40.4 IU/dL, 107.9 IU/dL, and 149.5 IU/dL
- No statistical difference between the means of both surveys by a paired t-test assuming unequal variances.
- The average relative difference between the results for individual laboratories was 14.6%, 9.7%, and 14.4%
- Some laboratories reported markedly different results between the two tests with the absolute difference in results ranging from 0 IU/dL to 104 IU/dL.

CONCLUSIONS

- NASCOLA laboratories generally performed well in the assessment of FXI in terms of inter-laboratory precision of samples with levels greater than 30 IU/dL.
- Result classification is generally performed well with samples FXI levels <40 IU/dL and ≥ 80 IU/dL; however, variability was observed for samples with FXI levels between 40 IU/dL and 80 IU/dLand elevated FXI levels.
- This study is limited by the lack of the data on specimens with very low levels of factor XI.