Birth weight and diazoxide unresponsiveness strongly predict the likelihood of congenital hyperinsulinism due to a mutation in ABCC8 or KCNJ11

**INTRODUCTION**

- Mutations in the KATP channel genes (ABCC8 & KCNJ11) cause ~80% of monogenic cases of congenital hyperinsulinism 1, 2
- Identifying a KATP channel mutation can inform on medical management 3
- Clinical features may help to establish the likelihood of a KATP channel mutation at diagnosis

**AIM**

Assess whether clinical features at presentation can predict the likelihood of a KATP channel mutation

**METHOD**

- Genetic testing of 1623 individuals with hyperinsulinism
- 761 individuals with KATP channel mutations
- 862 individuals without KATP channel mutations

Determine differences in clinical features

- Logistic regression modelling to determine most predictive features

**RESULTS**

<table>
<thead>
<tr>
<th>Birth weight (g)</th>
<th>Diazoxide responsive</th>
<th>Diagnosed first week of life</th>
<th>Insulin (pmol/l)</th>
<th>Female sex</th>
<th>Consanguineous</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>KATP</td>
<td>4333</td>
<td>127%</td>
<td>85%</td>
<td>162.2</td>
<td>46%</td>
<td>52%</td>
</tr>
<tr>
<td>Non-KATP</td>
<td>3512</td>
<td>88%</td>
<td>72%</td>
<td>115.4</td>
<td>36%</td>
<td>34%</td>
</tr>
<tr>
<td>P value</td>
<td>6 x 10^{-04}</td>
<td>2 x 10^{-02}</td>
<td>1 x 10^{-0}</td>
<td>1 x 10^{-0}</td>
<td>5 x 10^{-5}</td>
<td>2 x 10^{-12}</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- Birth weight and diazoxide response are highly predictive for congenital hyperinsulinism caused by KATP channel mutations
- Individuals born appropriate or large for gestational age who do not respond to diazoxide treatment are most likely to have a KATP channel mutation
- Thorough monitoring of clinical features at presentation in individuals with congenital hyperinsulinism can help to guide diagnosis, genetic testing, and future management

**REFERENCES**


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