Risk Indicators for Monitoring Hearing Loss in Infants: Who and Why?

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History of Risk Indicators:

- Initially introduced in 1973
- Need for early identification of hearing loss recognized, but technology not available for UNHS
- 5 criteria introduced to identify infants at risk for hearing loss
Risk Indicators for LOHL:

- Recommendations to monitor for late onset hearing loss (LOHL) made in 1982.
- 3 criteria initially identified
- Indicators added and clarified in 1990, 1994, 2000
- Specific list of indicators for LOHL first introduced in 1994
JCIH 2007 Position Statement

- Risk indicator categories collapsed due “to significant overlap among those indicators associated with congenital/neonatal hearing loss and those associated with delayed-onset/acquired or progressive HL”
- Indicators specific to LOHL noted
“All infants with or without risk factors requiring neonatal intensive care for greater than 5 days, including any of the following: ECMO, assisted ventilation, exposure to ototoxic medications (gentamycin and tobramycin) or loop diuretics (foresemid/lasix). In addition regardless of length of stay: hyperbilirubinemia requiring exchange transfusion.”
Current Risk Indicators

Year Introduced

1982
- Family history of childhood hearing loss*
- In-utero infection*
- Neurodegenerative diseases*

1990
- Postnatal infections*
- Assisted ventilation (current #3)
- Ototoxic meds or loop diuretics (current #3)

1997
- Craniofacial anomalies

1997
- Caregiver concern*
- Syndromes associated with hearing loss*

2000
- Physical Findings associated with a syndrome known to include a SNHL or permanent CHL
- Hyperbilirubinemia with transfusion (current #3)
- ECMO (current #3)*
- Head Trauma*

2007
- NICU > 5 days or any of the following regardless of length of stay:
  - Chemotherapy*
  *great concern for delayed onset hearing loss
Current Study

- To explore the impact of using the JCIH risk indicator criteria to identify children at risk for late onset hearing loss in our institution
- Retrospective review of prospectively collected database including information on specific risk indicators for all infants who received EHDI screen at the University of Michigan Medical Center from 2001-2007
University of Michigan EHDI Program

- Tertiary Care Hospital with Level III NICU
- Screenings done by trained audiology technicians using Biologic ABAER
- Program supervised by audiologist
- Technicians determine infants at risk for LOHL through case review and obtaining family history information from parent interview
Initial Hearing Screen Results
2001-2007

Eligible for Screening
26,341

Infants Remaining
25,612

Completed Screen
25,440

Pass initial screen
24,500

Refer on Initial Screen
940
(3.7% referral rate)

Hearing Loss identified
74
(2.8 per 1,000)

Infants not screened - 729
(Parent Refusal, transfer to birth hospital, patient expired)

Rescreened after refer
567
(60% of all referred)
Risk Indicators at U of M

- Family History of Hearing Loss
- Hyperbili with transfusion
- Ventilation > 14 days
- Bacterial Meningitis
- Perinatal infection
- Syndrome associated with HL
- ECMO
- Craniofacial Anomaly
- Ear pits/ tags
- Ototoxic medication exposure > 7 days
- Congenital Diaphragmatic Hernia*
- Low Birth Weight*

Protocol recommends evaluation every six months until preschool age.

*Not current JCIH risk indicator
Data Sources

- UM EHDI database maintained by EHDI staff. Database prospectively collected and includes screening/rescreen results and risk indicators for monitoring LOHL identified at time of discharge.
  - Of note, assisted ventilation only monitored when >14 days.
- NICU length of stay and administration of ototoxic medications determined through a query of hospital administrative and billing systems.
  - For infants transferred from/to outside facilities, data may underestimate NICU stay.
Question #1:

Does inclusion of all infants with NICU stay >5 days and any exposure to ototoxic medication significantly increase the number of infants being monitored?
Impact of Risk Indicator Criteria on Number of Infants Monitored

An additional 4300 babies (~600/year) would have been identified as at-risk.
Will Expansion of Criteria Capture More Children with Hearing Loss?

- 90 children have been identified with hearing loss from this data pool.
  - 74 congenital hearing loss
  - 16 late onset hearing loss
- All received newborn screen and diagnostic evaluation at University of Michigan.
UM Risk Indicators Identified in Presence of Congenital HL (n=74)

- 56 of 74 with Hearing Loss (75%) identified as at risk
- Total identified as at-risk for Hearing Loss: 1136 HI/Total Id'd = 4.9%

Bar chart showing various risk indicators: Family Hx, Hyperbili, Pulmonary, CDH, Meningitis, Perinatal Inf Syndrome, ECMO, VLBW, CFA, Other.
JCIH Risk Indicators Identified in Presence of Congenital HL (n=74)

JCIH criteria:
66 of 74 with Hearing Loss (89%) id’d as at risk
Total identified as at-risk: 5450
HI/Total Id’d = 1.2%
JCIH vs UM – Congenital HL

- JCIH identified 10 more babies with congenital hearing loss
- An additional 4214 babies identified at risk to capture additional 10 babies

If EHDI working, risk indicators not needed to capture congenital HL…what about LOHL?
Late Onset Hearing Loss

- 16 children identified with late onset hearing loss
- All 16 passed EHDI screen between 2001-2007
- Audiometric evaluations completed at University of Michigan confirm significant hearing loss.
For these 16 infants, none of the following risk indicators were identified at the time of discharge

- Congenital Diaphragmatic Hernia
- Craniofacial Anomalies
- ECMO
- Very Low Birth Weight
- UM Other (low apgars, hypoxic event)
Risk Indicators Identified in Presence of LOHL (n=16)
UM vs JCIH Criteria-LOHL

- JCIH identified 1 additional baby as at risk with LOHL.
- An additional 4300 babies were referred for monitoring to capture this additional infant.
Are these risk indicators accurate predictors for hearing loss?

- Expanding risk criteria is identifying more infants as at risk for hearing loss.
- Are some indicators better predictors than others?
- Is it possible to monitor fewer children without losing children at risk?
- To help answer these questions, an odds ratio was estimated for each risk indicator.
- Values >1 indicate increase odds (or risk)
## Odds Ratio of Congenital HL: UM Risk Indicators

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Family History of Hearing Loss</td>
<td>10.5 (5.1-21.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>58.3 (23.5-144.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pulmonary (Asst Vent &gt;14, PPHN)</td>
<td>14.2 (8.3-24.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Congenital Diaphragmatic Hernia</td>
<td>5.8 (0.8-40.8)</td>
<td>0.16</td>
</tr>
<tr>
<td>Bacterial Meningitis</td>
<td>28.4 (10.9-74.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Perinatal Infection</td>
<td>19.7 (2.9-132.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Syndrome associated with Hearing Loss</td>
<td>26.2 (13.9-49.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>ECMO</td>
<td>12.8 (4.8-34.3)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Very Low Birthweight</td>
<td>16.1 (6.1-42.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Craniofacial Anomalies</td>
<td>34.5 (18.5-64.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Other (low apgar, hypoxic event)</td>
<td>14.4 (7.1-29.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>All risk indicators combined</strong></td>
<td><strong>36.5 (24.0-55.7)</strong></td>
<td><strong>&lt; 0.0001</strong></td>
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Odds Ratio of UM Risk Indicators

- Except for CDH, all risk factors put infants at greater risk for hearing loss.
- Children with any of the risk indicators are over 36 times more likely to have hearing loss.
### Odds Ratio of Congenital HL: JCIH Risk Indicators

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<td>Craniofacial Anomalies</td>
<td>34.5 (18.5-64.6)</td>
<td>&lt; 0.0001</td>
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<tr>
<td>ICU &gt; 5 days</td>
<td>6.8 (4.5-10.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Loop Diuretic</td>
<td>3.9 (2.4-6.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>4.8 (3.2-7.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>All risk indicators combined</td>
<td>7.0 (4.4-11.1)</td>
<td>&lt; 0.0001</td>
</tr>
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Odds Ratio of JCIH Risk Indicators

- These indicators also result in increased risk for hearing loss.
- The magnitude of the increase in risk is noted to be lower than all the UM risk indicators (with the exception of CDH)
Adjusting for Other Risk Indicators

- It is not uncommon for infants to have more than one risk indicator.
- Multiple Logistic Regression Analysis was done to adjust odds ratios for other risk indicators.
## Unadjusted vs Adjusted: Congenital HL

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<th>Unadjusted OR (95% Confidence Interval)</th>
<th>Adjusted OR (95% Confidence Interval)</th>
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<tr>
<td>Family History of HL</td>
<td>10.5 (5.1-21.4) *</td>
<td>11.2 (5.0-25.1) §</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>58.3 (23.5-144.3) *</td>
<td>38.4 (10.2-144.7) §</td>
</tr>
<tr>
<td>Pulmonary (Vent&gt;14,PPHN)</td>
<td>14.2 (8.3-24.1) *</td>
<td>5.6 (2.5-12.4) §</td>
</tr>
<tr>
<td>Meningitis</td>
<td>**28.4 (10.9-74.1) ***</td>
<td><strong>15.6 (4.8-50.4) §</strong></td>
</tr>
<tr>
<td>Perinatal Infection</td>
<td>**19.7 (2.9-132.5) ***</td>
<td><strong>25.7 (3.2-206.8) §</strong></td>
</tr>
<tr>
<td>Syndrome Associated with HL</td>
<td>**26.2 (13.9-49.4) ***</td>
<td><strong>18.0 (8.2-39.4) §</strong></td>
</tr>
<tr>
<td>ECMO</td>
<td>**12.8 (4.8-34.3) ***</td>
<td><strong>2.9 (0.79-10.3) §</strong></td>
</tr>
<tr>
<td>Very Low Birth Weight</td>
<td>**16.1 (6.1-42.7) ***</td>
<td><strong>1.9 (0.50-7.3)</strong></td>
</tr>
<tr>
<td>Craniofacial Anomalies</td>
<td>**34.5 (18.5-64.6) ***</td>
<td><strong>29.1 (13.3-63.6) §</strong></td>
</tr>
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<td>Other (low apgar, hypoxic event)</td>
<td>**14.4 (7.1-29.4) ***</td>
<td><strong>5.0 (2.0-12.1) §</strong></td>
</tr>
<tr>
<td>ICU &gt; 5 Days</td>
<td>**36.5 (24.0-55.7) ***</td>
<td><strong>0.61 (0.29-1.3)</strong></td>
</tr>
<tr>
<td>Loop Diuretic</td>
<td>**6.8 (4.5-10.3) ***</td>
<td><strong>0.64 (0.31-1.3)</strong></td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>**3.9 (2.4-6.2) ***</td>
<td><strong>2.9 (1.7-5.1) §</strong></td>
</tr>
</tbody>
</table>

* Statistically significant at p < 0.05 for unadjusted analysis

§ Statistically significant at p < 0.05 for adjusted analysis
Unadjusted vs Adjusted Odds Risk: Congenital HL

- After controlling for other risk factors, the following were found to not increase the risk of hearing loss:
  - Congenital Diaphragmatic Hernia
  - Very Low Birth Weight
  - ICU length of stay > 5 days
  - Loop Diuretic Exposure
Removal of these indicators would reduce infants monitored as follows:

- **VLBW**: 24
- **Diuretic**: 347
- **ICU > 5**: 1073
- **ICU > 5 & Diuretic**: 209
- **CDH**: 1

Total = 1654
30% of all RI
## Odds Ratio of Late Onset HL: UM & JCIH Risk Indicators

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<tr>
<td>Family History of Hearing Loss</td>
<td>7.2 (0.95-54.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>83.1 (11.5-600.9)</td>
<td>0.013 *</td>
</tr>
<tr>
<td>Pulmonary (Asst Vent &gt;14, PPHN)</td>
<td>4.5 (0.59-33.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Meningitis</td>
<td>40.5 (5.5-300.2)</td>
<td>0.026 *</td>
</tr>
<tr>
<td>Perinatal Infection</td>
<td>124.7 (17.6-880.9)</td>
<td>0.0085 *</td>
</tr>
<tr>
<td>Syndrome associated with HL</td>
<td>52.3 (15.1-181.2)</td>
<td>&lt; 0.001 *</td>
</tr>
<tr>
<td><strong>UM All Risk Indicators Combined</strong></td>
<td><strong>22.6 (8.5-60.2)</strong></td>
<td>**&lt; 0.001 ***</td>
</tr>
<tr>
<td>ICU LOS &gt; 5 Days</td>
<td>0.76 (0.10-5.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Loop Diuretic</td>
<td>1.7 (0.38-7.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>5.7 (2.1-15.3)</td>
<td>0.0015 *</td>
</tr>
<tr>
<td><strong>JCIH All Risk Indicators Combined</strong></td>
<td><strong>5.0 (1.9-13.4)</strong></td>
<td>**0.0018 ***</td>
</tr>
</tbody>
</table>

*Statistically significant at p < 0.05

Risk indicators not associated with LOHL in this population excluded from this table, but not analysis (Congenital Diaphragmatic Hernia, ECMO, Birth weight, Craniofacial Anomaly, UM Other)
Odds Ratio of Late Onset HL: UM & JCIH Risk Indicators

- The following result in increased risk of late onset hearing loss:
  - Hyperbilirubinemia
  - Meningitis
  - Perinatal infection
  - Syndrome associated with hearing loss
  - Aminoglycoside exposure
**Unadjusted vs Adjusted: Late Onset HL**

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<td>9.4 (1.2-75.5) §</td>
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<tr>
<td>Hyperbilirubinemia</td>
<td>83.1 (11.5-600.9) *</td>
<td>72.4 (8.1-645.7) §</td>
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<tr>
<td>Meningitis</td>
<td>40.5 (5.5-300.2) *</td>
<td>13.6 (1.4-134.9) §</td>
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<td>Perinatal Infection</td>
<td>124.7 (17.6-880.9) *</td>
<td>125.1 (13.9-1123.5) §</td>
</tr>
<tr>
<td>Syndrome Associated with HL</td>
<td>52.3 (15.1-181.2) *</td>
<td>41.2 (10.2-167.0) §</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>5.7 (2.1-15.3) *</td>
<td>3.2 (1.1-9.4) §</td>
</tr>
</tbody>
</table>

Multiple logistic regression analysis includes risk indicators associated with an increased risk of late onset hearing loss with a p value < 0.2

* Statistically significant at p < 0.05 for unadjusted analysis
§ Statistically significant at p < 0.05 for adjusted analysis
Unadjusted vs Adjusted: Late Onset HL

- Each of these risk indicators is associated with an increased risk of late onset hearing loss.

- Given the low numbers, our confidence intervals for the magnitude of the risk increase are quite broad.
Conclusion

- These data do not support the inclusion of ICU stay >5 days and loop diuretic exposure as effective risk indicators for congenital or late onset hearing loss in our patient population.
- The number of infants referred for monitoring would be reduced by 30% by removing these indicators.
Further areas of study

- Relationship between aminoglycoside exposure and hyperbilirubinemia on LOHL
- Consideration of other risk indicators for LOHL
  - 6/16 with no risk indicator at discharge
- Examine risk indicators for larger numbers of children with LOHL
Special Thanks to Past & Present EHDI Staff for Collecting and Maintaining Data used in this Work

- Julie Carlson, AuD
- LuAnn Conant
- Colleen Hogan
- Donna Newell
- Suparna Malhotra, AuD
- Breena Scharrer, MS
- Janice Sinclair