Assessing the follow-up of BART hemoglobin reported by the Wisconsin Newborn Screening Laboratory

Bao Yang
MPH Candidate

Background

- The Wisconsin Newborn Screening (NBS) Laboratory screens 70,000 babies each year for 47 genetic disorders.

- Hemoglobin Disease
  - alpha thalassemia
  - (BART Hemoglobin)

- Argininosuccinic Acidemia (ASA)  
- Biotinidase Deficiency  
- Citrullinemia (Type I & II)  
- Congenital Adrenal Hyperplasia  
- Congenital Hypothyroidism  
- Cystic Fibrosis  
- Fatty Acid Oxidation (12)  
- Galactosemia  
- Hearing Screening  
- Hemoglobin S-Beta Thalassemia  
- Hemoglobin S/C Disease  
- Hemoglobin Variants  
- Homocystinuria  
- Hypermethioninemia  
- Hyperphenylalaninemia  
- Maple Syrup Urine Disease  
- Organic Acidemia (15)  
- Phenylketonuria  
- Sickle Cell Disease  
- Tyrosinemia (Type I, II & III)
Alpha thalassemia: Cause

- Deletion of the alpha chain gene which negatively affects the production of normal hemoglobin.
- A hemoglobin chain imbalance damages and destroys red cells, producing anemia.

Alpha thalassemia: Effects

Severity of alpha thalassemia depends on the number of alpha genes deleted.

1 gene deleted = silent carrier
2 genes deleted = mild or trait
3 genes deleted = hemoglobin H disease
4 genes deleted is fatal

No cure for alpha thalassemia
Objectives

To date, minimal follow-up has been undertaken.

Objectives of this study are:

1. To assess whether BART hemoglobin detected at birth actually resulted in a diagnosis of alpha-thalassemia.

2. To assess whether “High” BART hemoglobin detected at birth actually resulted in a diagnosis of alpha-thalassemia.

Dried Blood Spot Testing

- Blood from heel of newborn is taken
- Costs $69.50 (lab test $39.50, follow-up $30)
Newborn Screening Program for Hemoglobin

- The test for abnormal hemoglobins or “BART hemoglobin” is gel electrophoresis.
- Recommended follow up with primary care physician (PCP) at 6–12 months of age is a Complete Blood Count (CBC) and electrophoresis.
- Hematologic consultation is recommended for babies with Hemoglobin H disease, a severe form of alpha thalassemia.

One Study Year: 2006 Statistics

- 70,867 babies born in WI
- 2,392 (3.4%) Asian babies
- 39 (1.6%) BART reports issued on Asian babies
  - 38 Bart Hemoglobin, 1 High BART
Methods: Study Population

- 234 Hmong and other Asian babies with BART hemoglobin were born in Wisconsin between 2001 and 2006

- All babies were reported by NBS Laboratory as having BART hemoglobin

- 13 of these 234 babies were identified as “High” BART

Methods: Data Collection

- The PCP for each of the 234 subjects was identified

- Follow-up letter was sent to each PCP

- The PCP was asked to provide follow-up data including lab results

- PCPs who did not respond were telephoned
Methods: Data Coding

- Dr. Carol Diamond, UW hematologist, reviewed laboratory data and made a tentative diagnosis if none was reported.

- For the study, all information received was de-identified and entered into a Microsoft Excel database.

Response Rates

Follow up letter was sent 234 Cases where any information was received

Response rate: Initial mailing 65%
Response rate: After follow-up 83%

Information received
Diagnosis was reported 118 (50.5%)
Lost to follow up 104 (44.4%)
Undeliverable 8 (3.4%)
Pending 4 (1.7%)
### Lost to follow up (n=104)

#### Reasons for loss to follow-up

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>No response</td>
<td>38</td>
</tr>
<tr>
<td>Child no longer seen</td>
<td>31</td>
</tr>
<tr>
<td>Child never seen</td>
<td>25</td>
</tr>
<tr>
<td>No lab test performed</td>
<td>10</td>
</tr>
</tbody>
</table>

### Objective 1:

#### Diagnosis was reported (n=118)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha thalassemia</td>
<td>74</td>
<td>63%</td>
</tr>
<tr>
<td>Hemoglobin H disease</td>
<td>4</td>
<td>3%</td>
</tr>
<tr>
<td>Normal</td>
<td>15</td>
<td>13%</td>
</tr>
<tr>
<td>Anemia</td>
<td>8</td>
<td>7%</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>14%</td>
</tr>
</tbody>
</table>
### Diagnoses in the category “Other”

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other</td>
<td>17 (14%)</td>
</tr>
<tr>
<td>- BART Hemoglobin</td>
<td>12</td>
</tr>
<tr>
<td>- Beta thalassemia minor</td>
<td>1</td>
</tr>
<tr>
<td>- Delta beta thalassemia trait</td>
<td>1</td>
</tr>
<tr>
<td>- Failure to thrive</td>
<td>1</td>
</tr>
<tr>
<td>- Homozygous Hb E or E-B thalassemia</td>
<td>1</td>
</tr>
<tr>
<td>- Misinterpretation of lab report</td>
<td>1</td>
</tr>
</tbody>
</table>

### Objective 2:

**Assessing High BART babies (n=13)**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha thalassemia diagnosis confirmed</td>
<td>5</td>
</tr>
<tr>
<td>α-thalassemia</td>
<td>2</td>
</tr>
<tr>
<td>Hemoglobin H disease and α-thalassemia</td>
<td>1</td>
</tr>
<tr>
<td>α-thalassemia silent carrier</td>
<td>1</td>
</tr>
<tr>
<td>α-thalassemia in absence of iron lack</td>
<td>1</td>
</tr>
<tr>
<td>Other diagnosis reported</td>
<td>3</td>
</tr>
<tr>
<td>BART Hemoglobin</td>
<td>1</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>1</td>
</tr>
<tr>
<td>Microcytic anemia</td>
<td>1</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2</td>
</tr>
<tr>
<td>Pending</td>
<td>3</td>
</tr>
</tbody>
</table>
Conclusions

1. Reporting of the 13 High BART did not always result in a diagnosis of alpha thalassemia.
2. Detection of any level of BART hemoglobin led to the diagnosis of alpha thalassemia in 66% of babies.
3. Physician interpretation of the laboratory follow-up data was not consistent.
4. The number of babies lost to follow-up is substantial, possibly indicating physicians do not respond to reports of BART hemoglobin.

Potential Further Studies

- Assess information communicated to mothers when a finding of “High” BART or BART Hemoglobin is reported to the primary care provider.

- IRB approved 😊 (on the 4th try)
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