Prevention and Screening Thalassemia in Vietnam

Nguyen Hoang Nam
Area: 331,000 km²

Population: Over 90 million
- Urban: 30%
- Rural: 70%
- Man: 49%
- Women: 51%
- 54 ethnic groups

64 provinces/cities; 642 districts and 10,999 communes.
## Frequency of Beta Thalassemia and HbE

<table>
<thead>
<tr>
<th>Region</th>
<th>Ethnicty</th>
<th>n</th>
<th>(\beta)-thal.(%)</th>
<th>Hb E(%)</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>North</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinh-Hanoi</td>
<td></td>
<td>401</td>
<td>1.49</td>
<td>1.24</td>
<td>NC.Khanh et al, 1985</td>
</tr>
<tr>
<td>Kinh-</td>
<td></td>
<td>512</td>
<td>1.17</td>
<td>0.98</td>
<td>BQ.Tuyen et al, 1985</td>
</tr>
<tr>
<td>Tay</td>
<td></td>
<td>199</td>
<td>11.0</td>
<td>1.0</td>
<td>NC.Khanh et al, 1987</td>
</tr>
<tr>
<td>Muong</td>
<td></td>
<td>266</td>
<td>20.6</td>
<td>12.3</td>
<td>BV.Vien et al, 1998</td>
</tr>
<tr>
<td>Nung</td>
<td></td>
<td>42</td>
<td>7.1</td>
<td></td>
<td>NC.Khanh et al, 1987</td>
</tr>
<tr>
<td>Thai</td>
<td></td>
<td>236</td>
<td>11.4</td>
<td>20.03</td>
<td>TM.Cam et al, 2000</td>
</tr>
<tr>
<td>Middle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinh</td>
<td></td>
<td>35</td>
<td>2.55</td>
<td></td>
<td>LX.Chat et al, 1968</td>
</tr>
<tr>
<td>Pako</td>
<td></td>
<td>228</td>
<td>8.33</td>
<td>6.14</td>
<td>BQ.Tuyen et al, 1985</td>
</tr>
<tr>
<td>Van kieu</td>
<td></td>
<td>78</td>
<td>2.56</td>
<td>23.0</td>
<td>BQ.Tuyen et al, 1985</td>
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<tr>
<td>Ede</td>
<td></td>
<td>371</td>
<td>1.0</td>
<td>41.0</td>
<td>DB.Trucl et al, 1989</td>
</tr>
<tr>
<td>Se®ang</td>
<td></td>
<td>272</td>
<td></td>
<td>5.8</td>
<td>Bowman JE, 1971</td>
</tr>
<tr>
<td>Khmer</td>
<td></td>
<td>220</td>
<td></td>
<td>36.8</td>
<td>Bowman JE, 1971</td>
</tr>
<tr>
<td>Rhade</td>
<td></td>
<td>106</td>
<td></td>
<td>38.6</td>
<td>Bowman JE, 1971</td>
</tr>
<tr>
<td>South</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinh</td>
<td>HCM city</td>
<td>255</td>
<td>1.7</td>
<td>8.9</td>
<td>De’traverse et al, 1960</td>
</tr>
<tr>
<td>Kinh ( HCM city)</td>
<td></td>
<td>221</td>
<td>0.45</td>
<td>3.16</td>
<td>LX.Chat et al, 1968</td>
</tr>
<tr>
<td>Stieng</td>
<td></td>
<td>591</td>
<td></td>
<td>3.2</td>
<td>Blackwell, 1965</td>
</tr>
<tr>
<td>Cham</td>
<td></td>
<td>111</td>
<td></td>
<td>55.9</td>
<td>Bowman JE, 1971</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55</td>
<td></td>
<td>29.1</td>
<td>Bowman JE, 1971</td>
</tr>
</tbody>
</table>
Carrier of Thalassemia and haemoglobinopathies in Vietnam

✓ There hasn’t been a national epidemiology research yet.
✓ From separate recent study in last 5 years:

Carrier rate of

- Alpha thalassemia: 1.7% - 28%
- Beta thalassemia: 0.3% - 15.9%
- HbE: 0.4% - 35.6%

⇒ Total prevalence: about 10% -> 10 million carriers
⇒ Estimate 2000 major thalassemia new born per year
Beta thalassemia genes in the North

Nam NH et al, 2013
Beta Thalassemia genes in the South

Hoan NK et al, 2012
## Alpha Thalassemia genes in the north

<table>
<thead>
<tr>
<th>Mutation</th>
<th>SEA</th>
<th>Philipin</th>
<th>Thailand</th>
<th>α3.7</th>
<th>α4.2</th>
<th>HbQs</th>
<th>HbCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carriers</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>(n=39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>64.1</td>
<td>0</td>
<td>0</td>
<td>5.1</td>
<td>2.5</td>
<td>2.5</td>
<td>25.6</td>
</tr>
</tbody>
</table>

Ngoc ND et al, 2013
Thalassemia network

- Thalassemia centre in National Institute of Hematology and Blood Transfusion.
- Some big out patient clinic service were available in National Children’s Hospital, Children number 1 Hospital, Hematology and Blood transfusion Hospital Ho Chi Minh city, Central Hue Hospital
- In province hospital we have transfusion service but very variance.
# Thalassemia network

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute of Hematology and Blood Transfusion.</td>
<td>1500 cases</td>
</tr>
<tr>
<td>National Children’s Hospital</td>
<td>500 cases</td>
</tr>
<tr>
<td>Hematology and Blood transfusion Hospital Ho Chi Minh city</td>
<td>1000 cases</td>
</tr>
<tr>
<td>Central Hue Hospital</td>
<td>150 cases</td>
</tr>
</tbody>
</table>
Thalassemia Association and recent activities

- Vietnam Thalassemia Association (ViTA) has been established in February 2011.
- Cooperation with mass media for thalassemia
- Holding conference and training for patients/parent/ect
- Training courses for over 1000 include doctors, parents, patients, volunteer in 5 regions...
- Publish 4 books and leaveleft
- Raising fund for patients.
Prevention

• Awareness for community
• Screening
• Research epidemiology of Thalassemia and haemoglobinopathies in whole area Vietnam
• Genetic counseling
Prevention

Awareness for community

- Media: TV (O2TV), radio...
- Website: thalassemia.vn
- Leaflets
- Conferences/Seminars
- Professionals
Prevention

Screening:

- Pupil screening (in some research)
- High risk groups (relative with affected child)
- Pregnant women (in some program)
Prevention service

Genetic counseling and prenatal diagnosis in 3 hospital

- National Institute of Hematology and Blood Transfusion.
- National Children’s Hospital
- Tudu Hospital (obstetrics and gynecology)
Prevention service

1. NIHBT
   (National Institute of Hematology and Blood Transfusion)

National Children’s hospital

Blood Transfusion and Hematology hospital in Hochiminh city
Prevention Protocol

In community:
• Advice for couple to screening testing for Thalassemia
  ✓ Red cell osmotic fragility test
  ✓ DCIP
  ✓ FBC
  ✓ HPLC
• Premarital counseling if both of them are carrier
• If they get married → Prenatal Diagnosis
Prevention Protocol

In couple have one child with Thalassemia:
- Advice for couple testing for Thalassemia
  - FBC
  - HPLC
  - Mutation genes for thalassemia
- Counseling before they have second baby
Gene test

- ARMS PCR
  9 common mutation for Beta (cd41/41, cd17, cd71/72, cd26, IVS 1-1, IVS 1-5, IVS 2-625, -28, cd 95) and 7 for Alpha (SEA, Philipin, Thailand, \(\alpha3.7, \alpha4.2\), HbQs, HbCs)

- Strip assay
  Kit Strip Assay (Viennalab): 21 mutation alpha and 22 mutation of Beta

- Sequencing
## Screening in 944 high risk mothers

<table>
<thead>
<tr>
<th>Screening geneThalassemia</th>
<th>Carriers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>754</td>
</tr>
<tr>
<td>Father</td>
<td>385</td>
</tr>
<tr>
<td>Total</td>
<td>1139</td>
</tr>
</tbody>
</table>

*High risk mothers: low MCV*  
Ngo Diem Ngoc - NCH
Prenatal diagnosis

• Doing thalassemia gene for parents
• Let the wife have pregnant
• Contact with Obstetrics hospital to do aminofluid at 16 – 18 weeks
• CVS (Chorionic Villus Sampling) is not done in Vietnam because more risk for the fetus
• Abortion depend on the family
• The law is not prohibit it
## Prenatal diagnosis

### Prenatal diagnosis α và β thalassemia

<table>
<thead>
<tr>
<th></th>
<th>Fetus (%)</th>
<th>Normal (%)</th>
<th>Carriers (%)</th>
<th>Affected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb Bart’s</td>
<td>85 (27.3)</td>
<td>23 (27.0)</td>
<td>31 (36.4)</td>
<td>31 (36.4)</td>
</tr>
<tr>
<td>HbH</td>
<td>39 (12.5)</td>
<td>6 (15.3)</td>
<td>25 (64.1)</td>
<td>8 (20.5)</td>
</tr>
<tr>
<td>β thal</td>
<td>187 (60.1)</td>
<td>53 (28.3)</td>
<td>82 (43.8)</td>
<td>52 (27.8)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>311 (100)</strong></td>
<td><strong>82 (26.3)</strong></td>
<td><strong>138 (44.3)</strong></td>
<td><strong>91 (29.2)</strong></td>
</tr>
</tbody>
</table>
In 103 veteran hospital (Hanoi) since 2015

- One blastomere or trophectoderm was biopsied from day 3 or day 5 embryos after IVF-ICSI
- Embryo whole genome was amplified.
- Minisequencing and StripAssay were parallel performed to detect mutations.
- Unaffected embryos were selected for transfer.
Prevention and screening program for Hoa Binh province with government budget

• Awake Thalassemia for community in media: newspaper, TV, Radio, leaflet.
• Training for medical staffs
• Detect carriers in pupil and pregnancy
• Prenatal diagnosis
IV. PHÒNG BỆNH:
1. Phơi nhiễm màu da biếng mê bị liệt hồn nhiên
   - Thử màu để biết mình có là người mang
gen bệnh hay không.
   - Tư vấn để tránh kết hôn giữa
   hai người cùng mang gen bệnh.
2. Chẩn đoán trước sinh
   - Cẩn thận hạn chế mặc cả các lần chế thai để
   tránh gia đình đã có con bị bệnh nặng hoặc có
   vai trò để discern và định cùng lát người mang
   gen bệnh.

NGƯỜI BI BỆNH THALASSEMIA CẦN TƯ NGƯỜI
THAM GIA VÀO HỘI THALASSEMIA ĐỂ EUOC
QUẢN LÝ, TƯ VẤN VÀ HỖ TRỢ KHI CẦN THIỂT

Một địa chỉ dành cho trẻ bị bệnh
Thalassemia

Khoa Huyết học lâm sàng A9
Bệnh viện Nhi Trung ương
18/879 Đê La Thành - Đống Đa - Hà Nội
Tel: (04) 38343176 - (04) - 38343177
Số máy lẻ: 235
Prevention program for Hoa Binh province with government budget

• Total 9737 (7599 pupil, 2138 pregnancy) in 2013
  – HbE: 1148
  – β Thal carriers: 374
  – Patients: 38

• Prenal diagnosis 2012 – 2013 years: 45 cases
  • Normal: 12/45 (26.7%)
  • Carriers: 21/45 (46.7%)
  • Affected: 12/45 (26.7%)
Future Direction

• Doing genetic carrier research for each ethnic groups (on the way)

• Expanding prevention program in provinces with high prevalence

• National prevention program depend on economy of country