Report on Ten Years’ Experience of Premarital Hemoglobinopathy Screening at a Center in Antalya, Southern Turkey

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To cite this article: Duran Canatan & Serpil Delibas (2016): Report on Ten Years’ Experience of Premarital Hemoglobinopathy Screening at a Center in Antalya, Southern Turkey, Hemoglobin, DOI: 10.3109/03630269.2016.1170030

To link to this article: http://dx.doi.org/10.3109/03630269.2016.1170030

Published online: 20 May 2016.

Article views: 3

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SHORT COMMUNICATION

Report on Ten Years’ Experience of Premarital Hemoglobinopathy Screening at a Center in Antalya, Southern Turkey

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Abstract

Thalassemia and hemoglobinopathies are a major public health problem in Turkey. Hemoglobinopathy prevention programs (HPPs) were started in 33 provinces situated in Thrace, Marmara, Aegean, Mediterranean and South Eastern regions of Turkey in 2003. A premarital hemoglobinopathy test is mandatory and free of charge in this program. According to the Ministry of Health reports, 46 first level hemoglobinopathy diagnostic centers were established for premarital tests. Within the last 10 years, approximately 79.0% of married individuals per year were screened by the centers. While the percentage of premarital screening tests was 30.0% of all couples in 2003, it reached 86.0% in 2013. The number of newborn with thalassemia and hemoglobinopathies were 272 in 2002 and dropped to 25 in 2013. There has been a 90.0% reduction in affected births. Our hemoglobinopathy diagnostic center was established in 2003 and licensed by the Ministry of Health in 2004. We studied a total of 89,981 blood samples from premarital tests for 10 years and the incidence of β- and α-thalassemia (β- and α-thal) trait was found to be 6.57 and 3.56%, respectively. The distribution of the most common abnormal hemoglobins (Hbs) was: Hb S (HBB: c.20A > T) (0.31%), Hb D-Los Angeles (HBB: c.364G > C) (0.15%), Hb G-Coushatta (HBB: c.68A > G) (0.06%) and Hb E (HBB: c.79G > A) (0.02%). A total of 60 couples, both carrying β-thal trait, were directed to the prenatal diagnosis (PND) center in 10 years. The premarital hemoglobinopathy screening program is running successfully at our center and other centers in Turkey.

Keywords

Hemoglobinopathy, premarital screening, prevention

History

Received 3 November 2015
Revised 27 January 2016
Accepted 27 February 2016
Published online 19 May 2016

Thalassemia and hemoglobinopathies have been a major public health issue in the history of Turkey for 74 years (1). The first local public screening in Southern Turkey was performed by Aksoy et al. (2) in 1958. The overall incidence of β-thalassemia (β-thal) in the Turkish population was reported as 2.1% by Çavdar and Arcasoy (3) in 1971. The Turkish National Hemoglobinopathy Council (TNHC) was established in 2000 to combine all centers, foundations and associations into one organization together with the Ministry of Health (MOH). The MOH and TNHC picked up the screening results from 16 different cities in the Marmara, Aegean and Mediterranean regions between 1995 and 2000. A total 380,000 healthy subjects were screened in these provinces; an average frequency of 4.3% β-thal trait was found.

The regulations for the fight against hereditary blood diseases were published in 2002. The hemoglobinopathy prevention program (HPP) was started in 33 provinces situated in Thrace, Marmara, Aegean, Mediterranean and South Eastern regions by the MOH on May 8 2003, designated as World Thalassemia Day. According to the MOH reports, 46 first level hemoglobinopathy diagnostic centers were established for premarital tests (4).

Our hemoglobinopathy diagnostic center in Antalya, Southern Turkey, was established in 2003 and licensed in 2004. We report the results of our center for the past 10 years and evaluate the results of other centers in our country. Our hemoglobinopathy diagnosis center is the reference center in the Antalya region; therefore, blood samples were obtained from premarital screening, laboratories of private hospitals and other private laboratories. Our foundation has also performed hemoglobinopathy screening in schools and villages with permission from the MOH.

Complete blood count (CBC) and high performance liquid chromatography (HPLC) were implemented for hemoglobinopathy testing of the blood samples. Informed consent was obtained from all couples for premarital testing. Molecular analysis was done by amplification refractory mutation system–polymerase chain reaction (ARMS–PCR) or direct sequencing of globin chains at the Genetic Diagnostics Center or Mediterranean University Genetic Center in Antalya, Turkey. If couples both have β-thal trait, after genetic counseling, they are directed to the prenatal diagnosis (PND) center at the Mediterranean University in Antalya, Turkey. In 10 years, a total of 60 couples, both carrying β-thal...
trait, were directed to the Prenatal Diagnosis Center. In the
remaining couples, if only one person had β-thal trait, they
were not sent for PND.

A total of 118,575 blood samples were studied in 10 years;
89,981 of them (75.9%) were for premartial screening. The
incidence of β-thal trait, α-thalassemia (α-thal) trait and
abnormal hemoglobins (Hbs) in these samples were found to
be 6.57, 3.56 and 0.54%, respectively (Table 1). α-Thalassemia
was determined by molecular analysis in samples with low Hb
A2 levels after elimination of iron deficiency anemia. Most
abnormal Hbs were detected by HPLC, others were investigated
by molecular analysis such as ARMS-PCR or direct sequencing
of globin chains. The distribution of the most common
abnormal Hbs in all tests was Hb S (HBB: c.20A>T) (0.31%),
Hb D-Los Angeles (HBB: c.364G>C) (0.15%), Hb
G-Coushatta (HBB: c.68A>C) (0.06%) and Hb E (HBB:
c.79G>A) (0.02%), respectively.

The number of abnormal Hbs we found are as follows: 353
Hb S (48.4%), 178 Hb D-Los Angeles (24.4%), 71 Hb E
(9.7%), 25 Hb G-Coushatta (3.4%), 15 Hb C (HBB:
c.19G>A) (2.0%), 10 Hb D-Iran (HBB: c.67G>C) (1.3%),
six Hb Wayne [HBA2: c.420delE (or HBA1)] (0.8%), five Hb
J-Toronto [HBA2: c.17C>A (or HBA1)] (0.6%), four each for
Hb J-Baltimore (HBB: c.50G>A), Hb J-Anatolia (HBA2:
c.185A>C), Hb Willamette (HBB: c.155C>G) (0.5%), three
each for Hb O-Arab (HBB: c.364G>A), Hb South Florida
(HBB: c.4G>A), Hb P-Nilotic (β13-δ50 fusion) (0.4%), two
for Hb City of Hope (HBB: c.208G>A), Hb
N-Baltimore (HBB: c.286A>G), Hb G-Galveston (HBB:
c.131A>C), Hb Raleigh (HBB: c.5T>C), Hb J-Iran (HBB:
c.232C>G), Hb J-Meurer [HBA2: c.362C>A (or HBA1)],
Hb D-Ibadan (HBB: c.263C>A), Hb Dallas (HBA2:
c.294C>A), Hb Strumica [HBA2: c.338A>G (or HBA1)],
Hb Grady [HBA1: p.Thr119_Pro120insGluPhcThr (or
HBA2)], Hb Westmead (HBB: c.396C>G) (0.2%), one
each for Hb J-Daloa (HBB: c.172A>G), Hb Tarrant [HBA2:
c.379G>A (or HBA1)], Hb Akron (HBB: c.158A>T), Hb Q-
India (HBA1: c.193G>C), Hb Q-Thailand (HBA1:
c.223G>C), Hb Hasharon (HBA2: c.142G>C), Hb
Handsworth [HBA2: c.55G>C (or HBA1)], Hb Köln (HBB:
c.295G>A), Hb I-High Wycombe (HBB: c.178A>G), Hb
J-Chicago (HBA2: c.230C>A), Hb Richmond (HBB:
c.[309C>A or 309C>G]), Hb Osu Christiansborg (HBA1:
c.157G>A), Hb Hope (HBB: c.410G>A), Hb Toulon (HBB:
c.233C>A), Hb Rhode Island (HBA1: c.349C>T), Hb
Crete (HBA2: c.388G>C), Hb Fontainebleau [HBA2: c.64G>C (or
HBA1)] and Hb G-Waimanalo [HBA2: c.193G>A (or
HBA1)] (0.1%) (Table 2).

The World Health Organization (WHO) launched public
education, prospective screening programs, genetic counsel-
ing and PND for prevention of hemoglobinopathies in
Mediterranean countries in the 1970s. Premarital screening
studies have continued in Italy, Greece, England and Cyprus
since 1970 (5). Despite successful prevention of hemoglo-
binopathies in Mediterranean countries, hemoglobinopathies
are still a worldwide major health problem (6). Population
screening and prevention strategies continue in Eastern and
Middle East countries (7–10).

The first pilot premartial screening was published by Altay
et al. (11) in Mersin, Southern Turkey, and the incidence of
Hb S and β-thal was found to be 4.3 and 2.3%, respectively.
The second study was by Keskin et al. (12), in Denizli,
Western Turkey. They screened 19,804 healthy individuals
and found 2.6% β-thal trait and 0.11% sickle cell anemia
trait (Hb AS) (12).

Table 1. Premartial screening results of 89,981 blood samples.

<table>
<thead>
<tr>
<th>Blood samples</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-thal trait</td>
<td>591</td>
<td>6.56</td>
</tr>
<tr>
<td>α-thal trait</td>
<td>320</td>
<td>3.56</td>
</tr>
<tr>
<td>Abnormal Hbs</td>
<td>728</td>
<td>0.80</td>
</tr>
<tr>
<td>Total</td>
<td>9842</td>
<td>10.92</td>
</tr>
</tbody>
</table>

Table 2. The distribution of the most common abnormal hemoglobins in premartial screening tests (n = 724).

<table>
<thead>
<tr>
<th>Hb name</th>
<th>HbVar nomenclature</th>
<th>n</th>
<th>%</th>
<th>Hb name</th>
<th>HbVar nomenclature</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>HBB: c.20A&gt;T</td>
<td>353</td>
<td>48.4</td>
<td>HBA2</td>
<td>c.338A&gt;G (or HBA1)</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>D-Los Angeles</td>
<td>HBB: c.364G&gt;C</td>
<td>178</td>
<td>24.4</td>
<td>HBA1/p.Thr119_Pro120insGluPhcThr (or HBA2)</td>
<td>2</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>HBB: c.79G&gt;A</td>
<td>71</td>
<td>9.7</td>
<td>HBA2</td>
<td>c.369C&gt;G (or HBA1)</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>G-Coushatta</td>
<td>HBB: c.68A&gt;C</td>
<td>25</td>
<td>3.4</td>
<td>HBA2</td>
<td>c.172A&gt;G</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>C</td>
<td>HBB: c.79G&gt;A</td>
<td>15</td>
<td>2.0</td>
<td>HBA2</td>
<td>c.379G&gt;A (or HBA1)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>D-Iran</td>
<td>HBB: c.67G&gt;C</td>
<td>10</td>
<td>1.3</td>
<td>HBA2</td>
<td>c.158A&gt;T</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Wayne</td>
<td>HBA2: c.420delE (or HBA1)</td>
<td>6</td>
<td>0.8</td>
<td>HBA1</td>
<td>c.193G&gt;C</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>J-Toronto</td>
<td>HBA2: c.17C&gt;A (or HBA1)</td>
<td>5</td>
<td>0.6</td>
<td>HBA1</td>
<td>c.223G&gt;C</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>J-Baltimore</td>
<td>HBB: c.50G&gt;A</td>
<td>4</td>
<td>0.5</td>
<td>HBA2</td>
<td>c.142G&gt;C</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>J-Anatolia</td>
<td>HBA2: c.185A&gt;C</td>
<td>4</td>
<td>0.5</td>
<td>HBA2</td>
<td>c.55G&gt;C (or HBA1)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Willamette</td>
<td>HBB: c.155C&gt;G</td>
<td>4</td>
<td>0.5</td>
<td>HBA2</td>
<td>c.295G&gt;A</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>O-Arab</td>
<td>HBB: c.364G&gt;A</td>
<td>3</td>
<td>0.4</td>
<td>HBA2</td>
<td>c.230C&gt;A</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>South Florida</td>
<td>HBB: c.4G&gt;A</td>
<td>3</td>
<td>0.4</td>
<td>HBA2</td>
<td>c.309C&gt;A or 309C&gt;G</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>P-Nilotic</td>
<td>β13-δ50 fusion</td>
<td>3</td>
<td>0.4</td>
<td>HBA2</td>
<td>c.309C&gt;A or 309C&gt;G</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>City of Hope</td>
<td>HBB: c.208G&gt;A</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.157G&gt;A</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>N-Baltimore</td>
<td>HBB: c.286A&gt;G</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.410G&gt;A</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>G-Galveston</td>
<td>HBB: c.131A&gt;C</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.233C&gt;A</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Raleigh</td>
<td>HBB: c.5T&gt;C</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.349C&gt;T</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>J-Iran</td>
<td>HBB: c.232C&gt;G</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.388G&gt;C</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>J-Meurer</td>
<td>HBA2: c.362C&gt;A (or HBA1)</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.64G&gt;C (or HBA1)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>D-Ibadan</td>
<td>HBB: c.263C&gt;A</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.193G&gt;A (or HBA1)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Dallas</td>
<td>HBA2: c.294C&gt;A</td>
<td>2</td>
<td>0.2</td>
<td>HBA2</td>
<td>c.193G&gt;A (or HBA1)</td>
<td>1</td>
<td>0.1</td>
</tr>
</tbody>
</table>
According to the MOH reports, 46 first level hemoglobinopathy diagnostic centers were established in 41 cities for premarital tests in 2013. In the last 10 years, about 79.0% of married persons per year were screened by centers in Turkey (1,13). In recent years, premarital screening results have been published in some provinces from southern, middle, western and eastern regions of Turkey. Region, center and test numbers are summarized in Table 3. The mean incidence of β-thal and Hb AS was found to be 3.5 and 0.18%, respectively, in a total of 395,029 tests at these centers. While the incidence of thalassemia in our country is a common problem in the southern region, it was lower in the eastern and central regions (14–20). A total of 89,981 blood samples of premarital test were studied at our center, the incidence of β-thal trait was 6.57% and α-thal trait was 3.56%. In addition, 46 different abnormal Hbs were determined by HPLC and molecular analysis.

The overall incidence of hemoglobinopathies is 2.1 and 4.3% in coastal areas; the total population of Turkey is 78 million (1). The frequency of consanguineous marriages is 25.0% in the Turkish society, while it is 35.0% in families with hereditary blood disorders in Southern Turkey (21). The expected annual number of new patients with hemoglobinopathies was approximately 300 patients according to the calculations of population genetics. Indeed, there were 4513 hemoglobinopathy patients registered, with the number of newborn patients being 272 in 2002. The percentage of premarital screening tests was 30.0% of all couples in 2003 and reached 86.0% in 2013. Consequently, the number of affected newborns dropped to 25 in 2013. There has been a 90.0% reduction in affected births (1,13). We therefore conclude that the premarital hemoglobinopathy screening program is running successfully at our center and other centers in Turkey.

### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

### References


