Hemoglobin screening: response of a Brazilian community to optional programs

Triagem de hemoglobinopatias: resposta de uma comunidade brasileira a programas opcionais

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Abstract  The efficiency and the viability of three hemoglobin screening programs were investigated. They were offered on a voluntary basis to a Brazilian population and started with the analysis of blood donors, pregnant women and students. The hemoglobin screening was done through optional exams which included electrophoresis of hemoglobin and complementary hematological tests. A total of 13,670 people were tested over a period of 39 months and a total of 644 individuals with hereditary hemoglobin disorders were detected – 4.7% of the samples examined. The programs showed satisfactory indicators of viability and efficiency, expressed by the significative proportion of exams performed among the probands and their relatives.

Key words  Hemoglobinopathies; Genetic Screening; Genetic Counseling; Genetics

Resumo  Foram testadas a viabilidade e a eficiência de três programas de triagem de hemoglobinopatias. Os programas foram oferecidos voluntariamente a uma população brasileira e iniciaram com o exame de doadores de sangue, gestantes e escolares dos ensinos fundamental e médio. A triagem das hemoglobinopatias foi realizada mediante exames opcionais, representados pela eletroforese de hemoglobinas e exames complementares. Um total de 13.670 pessoas foram investigadas em um período de 39 meses, diagnosticando-se 644 portadores de alterações hereditárias da hemoglobina – 4,7% da amostra examinada. Os programas mostraram indicadores satisfatórios de viabilidade e de eficiência, expressos pela proporção significativa de exames realizados entre os propósitos e os seus parentes.

Palavras-chave  Hemoglobinopatias; Triagem Genética; Aconselhamento Genético; Genética
Introduction

Hemoglobinopathies, especially sickle cell syndromes, hemoglobin C, and β-thalassemia are common in Brazil because of the population’s ethnic composition (Salzano & Tondo, 1982; Ramalho, 1986; Naoum et al., 1987). Although the implementation of hemoglobinopathy programs in Latin America has been recommended by the World Health Organization (WHO, 1983), the Third World Academy of Science (TWAS, 1986), and the Pan-American Health Organization (OPS, 1987), systematic screening of heterozygotes for genetic counseling in Brazil is still very limited and is only performed in a few university centers. The WHO Committee for the Prevention and Control of Hemoglobinopathies has again recommended the implementation of community hemoglobinopathy programs in Latin America, especially in Brazil (Penchaszadeh, 1993).

Still, the success of a community hemoglobinopathy program depends on the population’s receptivity to such surveys. It is important to evaluate the results, since receptivity hinges on socioeconomic, psychological, and cultural factors. Indeed, as Bowman (1991) commented, population programs are often conceived in a theoretical, idealized world. In practice, however, they are carried out in the very different real world.

The present study focused on the efficiency of three voluntary hemoglobin screening programs developed in a Brazilian population, starting with blood testing in pregnant women, blood donors, and students.

Sampling and methods

The programs were developed in the State of São Paulo, whose population has an appreciable number of African (hemoglobins S and C) and Italian descendants (β-thalassemia). A total of 9,196 blood donors, 2,209 pregnant women, and 2,074 students were invited for screening at the State University of Campinas (Unicamp) over a period of 39 months. Blood donors and pregnant women were recruited at the university hospital and students at public schools in the community. Most of these individuals were of low socioeconomic status. Screening for hemoglobinopathies was performed by standard methods: complete blood count, hemoglobin electrophoresis in cellulose acetate-alkaline pH, red blood cell osmotic fragility, confirmation of β-thalassemia trait by increased Hb A2 fraction (Hb A2 quantification by the usual elution method, after electrophoresis), confirmation of hemoglobin S by solubility tests, and confirmation of fetal hemoglobin by the alkaline denaturation test (Ramalho, 1986). β-thalassemia was not investigated among blood donors, since this condition generally correlates with significant anemia. Cases that could not be diagnosed by these standard methods were submitted to specific tests, including DNA analysis. Molecular analysis was performed by DNA amplification (PCR) followed by restriction enzyme digestion and single-stranded conformational polymorphism analysis (SSCP).

Individuals were asked to participate voluntarily in the programs. Parental permission was required for high school students. Those found to be hemoglobin trait carriers were asked to bring their partners, parents, children (including newborns), and other relatives for investigation. All the above-mentioned tests were performed on these individuals.

Prenatal fetal diagnosis was not offered to high-risk couples, since Brazilian legislation forbids therapeutic abortion in these cases. All other laboratory tests, as well as medical treatment and genetic counseling, when necessary, were provided free of charge.

Individual and family interest in genetic counseling was evaluated objectively based on the percentage of screened heterozygotes who brought their partners, children, or other relatives for laboratory tests. They had received optional and individualized genetic counseling after evaluation by an interdisciplinary team consisting of geneticists, psychologists, and social workers. Genetic counseling had been completed with an identification card and explanatory booklet about hemoglobin disorders supplied to each subject.

Symptomatic individuals referred by physicians in the community were also tested (n = 185). Parents, siblings, partners, and children of positive hemoglobin disorder patients diagnosed in this group were invited for examination (n = 368). β-thalassemia trait was the main clinical hypothesis, followed by sickle cell syndromes.

Results

All blood donors and pregnant women, but only 54% of the students, agreed to be screened. A monthly average of 350 individuals, totaling 13,670 over the period (including probands and relatives) were investigated in the programs. A mean hemoglobin disorder prevalence of 4.7%
was observed. Table 1 shows the frequency of hereditary hemoglobin defects diagnosed in the population samples.

Fourteen cases of chronic hemolytic anemia (9 SS, 3 SC, 1 TT, and 1 CC) at ages from four months to 35 years (X = 9.8 years) are of special interest. Of the 630 heterozygotes, 378 were 15 years old or older, and of these, 228 (60%) agreed to receive genetic counseling. Rate of acceptance of genetic counseling was 64.5% among women and 50.6% among men ($\chi^2 = 4.29; 0.02 < p < 0.05$).

Twenty at-risk heterozygous couples (11 AS x AS, 5 AS x AC, 2 AT x AT, 1 AC x AC, and 1 AS x AT) were diagnosed. These couples had not received previous genetic counseling, and nine of them had a child with a clinically significant hemoglobinopathy (7 SS, 1 SC, and 1 CC).

As additional information from this study, four cases of persistent hereditary fetal hemoglobin and two cases of Camperdown hemoglobin were diagnosed by DNA analysis among the pregnant women.

Table 2 shows some program efficiency indicators.

Discussion

The first and perhaps most important aspect to emphasize when discussing this study is the high receptivity of a Brazilian community to health programs offered on a voluntary, non-coercive basis, as recommended by the São Paulo State Medical Code of Ethics (CREMESP, 1988). Programs showed satisfactory efficiency indicators, expressed by the significant proportion of tests performed. However, the program focusing on pregnant women was more effective than those screening blood donors and students, as evaluated by the percentage of relatives who volunteered for tests. The group of symptomatic individuals referred by physicians from the community was particularly useful for diagnosis of hemoglobin defects. This strategy thus deserves special attention in community-based programs.

### Table 1

<table>
<thead>
<tr>
<th>Population samples</th>
<th>AS</th>
<th>AT</th>
<th>AC</th>
<th>Hemoglobin defects</th>
<th>SS</th>
<th>TT</th>
<th>SC</th>
<th>CC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women (n = 2,209)</td>
<td>2.4</td>
<td>0.8</td>
<td>0.4</td>
<td></td>
<td>3.6</td>
<td></td>
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</tr>
<tr>
<td>Husbands* (n = 45)</td>
<td>2.2</td>
<td>2.2</td>
<td>4.4</td>
<td></td>
<td>8.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newborn children* (n = 60)</td>
<td>33.3</td>
<td>11.7</td>
<td>3.3</td>
<td></td>
<td>1.7</td>
<td>50.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other children* (n = 85)</td>
<td>37.6</td>
<td>5.9</td>
<td>9.4</td>
<td>1.2</td>
<td>1.2</td>
<td>55.3</td>
<td></td>
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</tr>
<tr>
<td>Siblings* (n = 260)</td>
<td>28.5</td>
<td>13.0</td>
<td>5.4</td>
<td>0.8</td>
<td></td>
<td></td>
<td>47.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood donors (n = 9,196)</td>
<td>1.0</td>
<td></td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
</tr>
<tr>
<td>Spouses* (n = 30)</td>
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<td></td>
<td>3.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13.3</td>
</tr>
<tr>
<td>Children* (n = 61)</td>
<td>45.9</td>
<td>1.6</td>
<td></td>
<td></td>
<td>3.3</td>
<td>50.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Students (n = 1,118)</td>
<td>0.6</td>
<td>1.2</td>
<td>2.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Parents and siblings* (n = 53)</td>
<td>7.5</td>
<td>37.7</td>
<td></td>
<td></td>
<td>45.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-Total (n = 13,117)</td>
<td>2.4</td>
<td>0.8</td>
<td>0.5</td>
<td>0.3</td>
<td>0.01</td>
<td>3.74</td>
<td></td>
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</tr>
<tr>
<td>Individuals referred by physicians and relatives (n = 553)</td>
<td>11.2</td>
<td>13.4</td>
<td>3.0</td>
<td>0.9</td>
<td>0.5</td>
<td>29.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n = 13,670)</td>
<td>2.7</td>
<td>1.3</td>
<td>0.6</td>
<td>0.07</td>
<td>0.01</td>
<td>0.02</td>
<td>0.01</td>
<td>4.71</td>
<td></td>
</tr>
</tbody>
</table>

AS = sickle cell trait; AT = β-thalassemia trait; AC = hemoglobin C trait; SS = sickle cell anemia; TT = β-thalassemia major; SC = hemoglobin SC disease; CC = hemoglobin C disease.

* Relatives of heterozygotes.

### Table 2

<table>
<thead>
<tr>
<th>Program efficiency indicators.</th>
<th>Pregnant women</th>
<th>Blood donors</th>
<th>Students</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance (%)</td>
<td>100</td>
<td>100</td>
<td>54</td>
</tr>
<tr>
<td>Partner testing (%)</td>
<td>56</td>
<td>33</td>
<td>-</td>
</tr>
<tr>
<td>Parent testing (%)</td>
<td>-</td>
<td>-</td>
<td>65</td>
</tr>
<tr>
<td>Testing of children and/or other relatives (%)</td>
<td>90</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>Mean number of individuals examined for each heterozygote</td>
<td>5.6</td>
<td>0.76</td>
<td>2.4</td>
</tr>
</tbody>
</table>

* Relatives of heterozygotes.
Prenatal screening for hemoglobinopathies has several pragmatic advantages (Rowley et al., 1991). Pregnant women already have routine blood tests in the prenatal period, and during pregnancy women are more aware of their own health and that of their children. Prenatal screening for hemoglobinopathies in other countries, such as the United States (Rowley et al., 1991), Cuba (Granda et al., 1991), Greece (Loukopoulos, 1985), Canada (Scriver et al., 1984), and Italy (Tentori & Marinucci, 1983) also provided satisfactory results. However, these programs conducted in the Northern Hemisphere included the possibility of fetal diagnosis and optional therapeutic abortion in their objectives. The advantages and disadvantages of prenatal screening for hemoglobinopathies have been thoroughly discussed by Bowman (1991) and Loader et al. (1991).

Population screening is extremely valuable for initiating early treatment, and in this case families may become fully prepared for the management of babies with serious hemoglobinopathies. Some societies offer prenatal diagnosis, but even if this is not the case, in Brazil there are enormous advantages to such educational programs.

Acceptance of optional genetic counseling by heterozygotes (60%) was considered satisfactory and was significantly higher amongst women. However, it was lower than that observed by Rowley et al. (1991) in the Rochester program in the United States (69%) ($\chi^2 = 4.94; 0.02<p<0.05$). Since the genetic counseling offered in the Campinas programs had essentially educational objectives, a complementary instruction leaflet was given to heterozygotes, explaining their hemoglobin defect in detail. According to Kessler (1989), genetic counseling programs are more efficient when the goals are educational rather than eugenic. The most gratifying short-term result of the programs in Campinas was the increased community awareness concerning hemoglobin disorders.

From the clinical point of view, another gratifying result was the diagnosis and treatment of 14 cases of chronic hemolytic anemia and 178 β-thalassemia trait carriers, many with hypochromic and microcytic anemia. Although hemoglobinopathies are not curable, they are treatable, resulting in improved quality of life for patients. For example, such simple measures as vaccination and prophylactic administration of penicillin to children with sickle cell syndromes increase their life expectancy (Vichinsky et al., 1988; Wong et al., 1992). Neonatal screening is thus an option for early treatment of hemoglobinopathies.

Finally, the programs’ cost/benefit relationship deserves to be highlighted. At a cost of only US$1.10 per person the programs were able to screen a large number of people and achieve increased community awareness concerning hemoglobin disorders.

References


