

GENETICS AND PUBLIC HEALTH: RESPONSE OF A BRAZILIAN POPULATION TO AN OPTIONAL HEMOGLOBINOPATHY PROGRAM

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ABSTRACT

The efficiency and viability of a hemoglobinopathy program was investigated. The program was offered on a voluntary basis to a Brazilian community (Araras, SP) and started with the blood analyses of pregnant women. A total of 2209 pregnant women were screened in the first 39 months and 80 heterozygotes were diagnosed (52 AS, 19 AT and 9 AC). Another 1003 persons related to these heterozygotes were examined and a total of 432 heterozygotes were diagnosed (241 AS, 140 AT and 51 AC), added to 13 patients with chronic hemolytic anemia (8 SS, 3 SC, 1 TT and 1 CC) and 16 risk couples, made up of two heterozygotes. The examination percentages of pregnant women (100%), newly born children (75%), other children (97%), husbands (56%) and other relatives (64%) showed the high rate of acceptance of the program in the community. Genetic counselling was accepted by 60% of the heterozygotes over 15 years of age.

INTRODUCTION

Hemoglobinopathies, especially sickle cell syndromes, hemoglobin C and beta thalassemia are common in Brazil because of the ethnic composition of the population (Salzano and Tondo, 1982; Zago and Costa, 1985; Ramalho, 1986; Naoum *et al.*, 1987). Although the implantation of hemoglobinopathies programs in Latin America has been recommended by the World Health Organization (WHO, 1983), by the Third World Academy of Science (Twas, 1986) and by the Panamerican Health Organization (OPS, 1987), the systematic screening of heterozygotes for clinical genetical orientation in Brazil is still very limited, being carried out by only a few university centers. The Committee for the Prevention and Control of Hemoglobinopathies of the World Health Organization has again recommended the implantation of community hemoglobinopathies programs in Latin America, especially in Brazil (Penchaszadeh, 1993).

The success of a community hemoglobinopathies program depends on the receptivity of the population to studies of this kind. It is important to evaluate the results, as receptivity depends on socio-economic, psychological and cultural factors. Indeed, as Bowman (1991) comments, populational 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 investigated the viability and efficiency of a voluntary hemoglobinopathies program developed in a Brazilian community, starting with the blood examination of pregnant women.

SAMPLING AND METHODS

The program was developed in Araras, São Paulo State. The town has 87,355 inhabitants, a monthly *per capita* earnings of US\$ 392, 100% sewage service and an infant mortality rate of 20:1000 (IBGE, 1992). The conditions are theoretically ideal for a hemoglobinopathies program because there is a single maternity hospital and a centralized pre-natal care service in five town public health clinics and a few private practices. The population also has an appreciable number of negroes (hemoglobins S and C) and Italian descendants (beta thalassemia).

A total of 2209 pregnant women were examined in a period of 39 months. Of those, 1478 had their pre-natal care in the five public clinics and 731 in private clinics. The hemoglobinopathies investigation was carried out by hemogram, electrophoresis of hemoglobins in cellulose acetate, alkaline pH, test of osmotic fragility of the red blood cells, confirmation of the S hemoglobin by solubility, confirmation of the beta thalassemia trait by the A₂ hemoglobin quantification by elution and confirmation of the fetal hemoglobin by the alkaline denaturation test. A blood sample from cases that could not be diagnosed by

these basic methods was sent to UNICAMP, for specific tests, including DNA analysis.

Pregnant women were asked to participate voluntarily in the program. Those found to be hemoglobin trait carriers were asked to bring their husbands, children, including newly born, and other relatives, for examination. People who came voluntarily or who were indicated by doctors in the city were also examined. All the fore mentioned tests were carried out on these individuals.

The pre-natal diagnosis was not offered to high risk couples as Brazilian legislation forbids therapeutic abortion in these cases. All the other laboratory exams, as well as medical treatment and genetic counselling, when necessary, were provided free of charge.

RESULTS

A monthly average of 82 individuals, totalling 3212 people, were examined in the program. An average index of 13.8% positive hemoglobinopathies cases was observed. Table I shows the frequency of hereditary

hemoglobinopathies diagnosed in the total sample. Thirteen cases of chronic hemolytic anemia at ages from four months to 35 years ($\bar{x} = 9.8$ years) are of special interest. Of the 432 heterozygotes, 261 were 15 years old or older and, of these, 158 (60.5%) accepted genetic orientation. The rate of acceptance of the genetic counselling was $120/186 = 64.5\%$ among the women and $38/75 = 50.6\%$ among the men ($\chi^2 = 4.29$; $0.02 < P < 0.05$).

Sixteen risk couples, made up of two heterozygotes (8 AS x AS, 5 AS x AC, 2 AT x AT and 1 AC x AC), 12 of which still at reproductive age were examined. These couples had not received previous genetic counselling and five of them already had a child with a clinically significant hemoglobinopathy (3 SS, 1 SC, 1 CC).

As a complementary piece of data to this study, outside the objectives of Public Health, four cases of persistent hereditary fetal hemoglobin and two cases of Camperdown hemoglobin, were diagnosed by DNA analysis at the Hemocenter at UNICAMP.

Table II shows some indicators of the viability and efficiency of the program.

Table I - Diagnosed hemoglobinopathies in the random sample.

Groups	Pregnant women (N=2209)	Husbands (N=45)	Newly born children (N=60)	Other children (N=85)	Other relatives (N=260)	Non relatives (N=553)	Total (n=3212)
Hemoglobinopathies							
AS	2.4%	2.2%	33.3%	37.6%	28.5%	11.2%	7.5%
AT	0.8%	2.2%	11.7%	5.9%	13.0%	13.4%	4.4%
AC	0.4%	4.4%	3.3%	9.4%	5.4%	3.0%	1.6%
SS				1.2%	0.8%	0.9%	0.2%
TT			1.7%				0.03%
SC						0.5%	0.09%
CC				1.2%			0.03%
Total	3.6%	8.8%	50.0%	55.3%	47.7%	29.0%	13.8%

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

Table II - Program viability and efficiency indicators.

Indicator	Public health clinics	Private clinics
Examination acceptance by the pregnant women	100%	100%
Positive index in heterozygote pregnant women	3.6%	3.5%
Husband examination	65%*	38%*
Newly born examination	74%	77%
Examination of other children	96%	100%
Examination of other relatives	69%	54%
Positive rate of the hemoglobinopathies among relatives	47%	43%
Average number of people examined tracing to each heterozygote pregnant woman	5.8	5.2

*Significant difference by χ^2 , at the 5% level of probability.

DISCUSSION

The first and perhaps the most important aspect to emphasize when discussing this study is the high receptivity of a Brazilian community to a health program offered in a voluntary, not enforced basis, as recommended by the Medical Code of Ethics (CREMESP, 1988). Starting the program with the examination of pregnant women may have had a positive influence on the results. The pre-natal screening for hemoglobinopathies has several pragmatic advantages (Rowley *et al.*, 1991). The pregnant woman already have routine hemograms in the pre-natal treatment, and during pregnancy a woman is more aware of her own and her children's health. Pre-natal screening for hemoglobinopathies carried out in other countries, such as in the U.S.A. (Rowley *et al.*, 1991), Cuba (Granda *et al.*, 1991), Greece (Loukopoulos, 1985), Canada (Scriver *et al.*, 1984), Italy (Tentori and Marinucci, 1983) and England (Anionwu *et al.*, 1988) also obtained satisfactory results. These Northern Hemisphere programs, however, included the pre-natal diagnosis of the fetus and possible therapeutic abortion in their objectives. This eugenic objective has not always been attained by these programs, as Loader's *et al.* (1991) work in the U.S.A. illustrates. The advantages and disadvantages of eugenic pre-natal screening for hemoglobinopathies have been widely discussed by Bowman (1991).

The positive index of heterozygotes observed among the examined pregnant women (3.6%) and the percentage of heterozygote pregnant women who brought their husband for examination (56%) were very similar to those observed in the program carried out in Rochester, U.S.A. by Rowley *et al.* (1991) (4.3% and 55%, respectively).

As shown in Table II, the indicators of viability and efficiency of the program did not differ significantly between the low socio-economic level population treated at the public health clinics and the higher socio-economic level treated in the private clinics. The only exception was the percentage of husbands examined, which was higher in the public health clinics (65%) than in the private clinics (38%) ($\chi^2 = 4.95$; $P = 0.026$). This result shows that high socio-economic and school level is not such a favorable factor in these programs as would have been expected. According to Ramalho *et al.* (1992), people's feelings frequently count more in the genetic field than their intellect.

The proportion of hemoglobin S and C was greater among heterozygote pregnant women diagnosed at the public health clinics (48/54 = 88.9%) than that at the private clinics (13/26 = 50%) due to the greater participation of negroids in the first sub-sample. The proportion of beta thalassemia trait carriers was significantly higher among the heterozygotes detected in the private clinics (13/26 =

50%) than in the public health clinics (6/54 = 11%), showing the greater participation of Italian descendants in this sub-sample ($\chi^2 = 14.65$; $P < 0.001$).

The acceptance of genetic counselling offered optionally to the heterozygotes (60.5%) was considered satisfactory and was significantly greater among women. It was lower, however, than that observed by Rowley *et al.* (1991) in the North American program at Rochester (69%) ($\chi^2 = 4.94$; $0.02 < P < 0.05$). As the genetic counselling offered in the program was essentially educational in its objectives, an instruction leaflet was given to the heterozygotes, explaining their hemoglobin alteration in detail. Kessler (1989) showed that genetic counselling programs are more efficient in educational rather than eugenic objectives.

When a hemoglobinopathy program is set up in a community of the size of Araras, SP, it is inevitable and even desirable that some people use it spontaneously or that they be sent by their doctors. In this study, besides the pregnant women and their relatives, 553 other people, with a hemoglobinopathy rate of 29%, used the program.

The most gratifying result of the program was the diagnosis and treatment of 13 cases of chronic hemolytic anemia and of 140 carriers of the beta thalassemia trait, many with hypochromic and microcytic anemia. Hemoglobinopathies, while incurable, are treatable resulting in the improvement of the patients' quality of life. Some simple measures, such as vaccination and prophylactic administration of penicillin to children with sickle cell anemia increases, their life expectancy (Vichinsky *et al.*, 1988; Wong *et al.*, 1992).

To conclude, it is worth mentioning the cost benefit relationship of the program carried out in Araras, SP. A yearly expense of only US\$ 3000 allowed the care of a large number of people and the education of the community.

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RESUMO

Investigou-se a viabilidade e a eficiência de um programa de hemoglobinopatias oferecido em caráter opcional a uma comunidade brasileira (Araras, SP) abordada a partir das gestantes. Nos primeiros 39 meses foram triadas 2209 gestantes, diagnosticando-se 80 heterozigotas (52 AS, 19 AT e 9 AC). A partir dessas heterozigotas foram examinadas outras 1003 pessoas, diagnosticando-se um total de 432 heterozigotas (241 AS, 140 AT e 51 AC), 13 doentes com anemia

hemolítica crônica (8 SS, 3 SC, 1 TT e 1 CC) e 16 casais de risco, constituídos por dois heterozigotos. As porcentagens de exame de gestantes (100%), de recém-nascidos (75%), de outros filhos (97%), de maridos (56%) e de outros parentes (64%) indicaram uma boa aceitação do programa pela comunidade. O aconselhamento genético foi aceito por 60% dos heterozigotos com mais de 15 anos de idade.

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