2013

Delivering Genetic Education and Genetic Counseling for Rare Diseases in Rural Brazil

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10.1007/s10897-013-9570-x

Journal of Genetic Counseling

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--Manuscript Draft--

Manuscript Number:	
Article Type:	Genetic Counseling: A Global Perspective
Keywords:	Genetic education; genetic counseling; rare diseases; founder effect; endogamy; consanguinity; MPS VI
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Delivering genetic education and genetic counseling for rare diseases in rural Brazil

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Running title: Genetic education and genetic counseling in Brazil

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Abstract

Brazil is the largest country in Latin America, with an ethnically diverse, Portuguese-speaking and predominantly Roman Catholic population of some 194 million. Universal health care is provided under the Federal Unified Health System (*Sistema Único de Saúde*) but, as in many other middle and low income countries, access to medical genetics services is limited in rural and remote regions of the country. Since there is no formally recognized Genetic Counseling profession, genetic counseling is provided by physicians, trained either in medical genetics or a related clinical discipline. A comprehensive medical genetics program has been established in Monte Santo, an inland rural community located in the state of Bahia in Northeast Brazil, with high prevalences of a number of recessive genetic disorders, including non-syndromic deafness, phenyketonuria, congenital hypothyroidism and mucopolysaccharidosis VI (Maroteaux-Lamy syndrome). Genetic education, counseling and treatment are locally provided, with a neonatal screening program for MPSVI currently under trial.

Introduction

By global standards Brazil is a huge country with a land area of 8.54 million km^2 and a population of 194.3 million, which makes it both the largest country in Latin America and the fifth most populous country world-wide. As summarized in Table I, in economic and health terms Brazil is a middle ranked country with an adult literacy rate of 88.6%, a mean annual per capita income of US$11,000, and 84% of its population living in urban centres. The introduction of birth control programs by the Federal Government in the 1990s resulted in a marked slowing of the annual population growth rate, and the total fertility rate is now 1.9, i.e. below the replacement rate. However, in terms of its age profile Brazil remains a young country, with 25% of the population under 15 years and just 7% over 65 years (PRB, 2012).

Health care in Brazil

The majority of the population is served by the public Unified Health System (*Sistema Único de Saúde* or SUS), which was established in 1988 to ensure equitable access to health for all citizens and is one of the largest public health systems in the world (Brazil, 1990). SUS is organized on a municipal basis, with management provided at state level and financial support from the Federal Ministry of Health. Health expenditure in Brazil in 2007 comprised 8.4% of Gross Domestic Product (WHO, 2010), with 1.84 medical practitioners and 2.26 hospital beds per 1,000 of the population (IBGE, 2009).

The most recent available national statistics indicate neonatal, infant and under-5 year deaths rates of 11/1,000, 20/1,000 and 22/1,000 respectively, while non-communicable diseases now account for 74% of deaths (Table I). The shift to a non-communicable disease profile in Brazil also is reflected in the reported causes of early deaths. In 1980, 38% of infant deaths were ascribed to perinatal causes, with congenital anomalies listed as the fifth most common cause of

death and representing just 5% of the total. Given proportional reductions in infectious, nutritional, and respiratory diseases, by 2000 congenital malformations had became the second most common cause of deaths in children under age 1 year representing 13% of the total, and by 2006 mortality due to congenital defects had risen to 16.3% of all infant deaths (Brazil, 2010)

[Table I here]

Ethnicity of the Brazilian population

A question on ethnicity was included in the 2000 Census of Brazil, with the options of White, Black, *Pardo* (mixed color or race; mulatto or *mestizo*), Asiatic, and Native Brazilian Indian. Of those who responded, 54.0% self-declared as White, while 39.9% were *Pardos*, 5.4% Black, 0.5% Asiatic, and 0.2% Native Indians. Persons of African ancestry, represented by those who self-declared as Black or *Pardo* were mainly resident in the North (69.0%) and Northeast (65.8%), whereas the highest percentages of Whites were located in the Southeast (62.4%) and South (83.6%) regions of the country (IBGE, 2000).

Medical genetics services in Brazil

Most Brazilians do not have access to medical genetic services, as the majority of these services are concentrated in tertiary centers located in the most developed Southeast and South regions of the country. A number of institutions have sophisticated laboratory infrastructures and offer diagnostic testing, including cytogenetic and molecular genetic analyses. Specialists in medical genetics tend to aggregate within the major service centers located in the Center-South of the country, which in practice means that a majority of Brazilian states have few or no resident trained professionals in clinical genetics (Horovitz et al., 2012).

Since access to specialist medical genetics services has been limited, the establishment of regional services and the promotion of genetics within primary care were identified as priority

issues (Marques-de-Faria et al., 2004; Penchaszadeh, 2004). In response, the Federal government formulated a national policy for comprehensive clinical genetics services, which included both specialist medical genetics centers and the inclusion of genetics in primary care programs (Brazil, 2009). In the latter setting the policy provides for the identification and follow-up of families with congenital anomalies and genetically determined diseases, but as yet progress in meeting its stated aims has been slow.

Medical genetics training

By comparison with other clinical specialities, Medical Genetics is a relatively young branch of medicine in Brazil with Board Certification in Medical Genetics the responsibility of the Brazilian Society of Medical Genetics (Sociedade Brasileira de Genética Médica, SBGM). Eleven postgraduate residency programs each of three years' duration have been approved by the National Medical Residency Committee (Comissão Nacional de Residência Médica, 2006), all co-located with specialist laboratory services in the Center-South of the country (Secretaria de Educação Superior, 2009). Professional accreditation in Medical Genetics also can be awarded by other medical specialties, e.g. pediatrics, subject to approval by the Brazilian Medical Association and the Federal Council of Medicine. During the last 30 years a combined total of some 200 physicians have been awarded Board Certification in Medical Genetics through one or other of these systems.

Genetic counseling

Although health professionals from many backgrounds are involved in providing genetic services in Brazil, the profession of Genetic Counselor is not formally recognized and so the provision of genetic counseling is almost exclusively restricted to physicians. However, many groups, centers and services coordinated by physicians offer informal, non-accredited training

programs in genetic counseling to health care professionals drawn from a range of different health disciplines, mainly nursing and psychology (Brunoni, 2002). Prior to a medical genetics consultation, clients may be interviewed by a non-physician, most commonly health professionals with a psychology background, who provide information on the investigations that may be undertaken as part of their diagnosis and treatment.

Genetic education and genetic counseling for inherited disorders in a rural setting

Given the concentration of medical genetics resources in the Center-South of the country, specific problems in dealing with inherited disorders in less privileged rural communities commonly are encountered. As an example, the inland municipality of Monte Santo is located in the state of Bahia, northeast Brazil, some 350 km from Salvador the state capital. According to the 2010 Census of Brazil the total population of Monte Santo was 52,338, scattered across some 200 villages.

By comparison with the national average Monte Santo is a poor community, with an average annual per capita income of just US$1,403 and 66% adult literacy, and it is served by a single general hospital with 60 beds (IBGE, 2010). Monte Santo was established mainly by Portuguese settlers at the end of the 18th century but with substantial Native Indian Amerindian and African admixture. Therefore in the 2010 Census respondents self-identified as 37.6% White, 57.2% *Pardo*, and 5.2% Black (IBGE, 2010).

A cluster of cases of mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy syndrome) was provisionally identified in Monte Santo, but there was no information on the prevalence of the disorder, which in other parts of the world is regarded as rare with reported incidence rates ranging from 1/43,261 in Turkey to 1/1.51 million births in Sweden (Valayannopoulos et al., 2010). To investigate the feasibility of establishing genetic services in this generally under-

provided community, in 2006 a preliminary scoping visit to Monte Santo was arranged to meet with the local civil authorities, medical staff and local residents. Following this visit a multidisciplinary project *Genetics in the Sertão* was initiated as a partnership between public and private institutions. The aim of the project was to create a coordinated genetic education, genetic counseling, treatment and screening program for inherited disorders in the community, with oversight provided by a multidisciplinary team of health care professionals, including medical geneticists.

It soon became obvious that the prevalence of MPS VI in Monte Santo was indeed high with 13 living cases identified in 11 nuclear families, and genetic analysis showed that all affected persons were homozygous for the p.H178L mutation in the arylsulfatase B (ARSB) gene (Costa-Motta et al., 2011). The data therefore strongly suggested the expression of a founder mutation, maintained and spread through intra-community and intra-familial marriage and resulting in a present-day MPS VI prevalence of 1/5,000. On the basis of these results, and with the knowledge that other inherited disorders, including non-syndromic deafness, phenylketonuria and congenital hypothyroidism, appeared to have an increased prevalence in the Monte Santo community, the *Genetics in the Sertão* project was established as an ongoing, community-based program.

Genetic education

In Brazil, the Community Health Agents Program was established in 1991 as part of the Family Health Program. It is seen as an important facet of primary health care strategy, with community health agents (CHA) trained to identify, refer, guide and follow-up families in their community (Brazil, 2000). As part of the *Genetics in the Sertão* initiative in Monte Santo, lectures, workshops and assessments of their training are regularly organized for the CHA, with

information on the diseases thought to be most prevalent in the community, reinforcement of the importance of early diagnosis, instruction on eliciting relevant information from families, and accessing medical advice and appropriate treatment. As community members, the involvement of the CHA is fundamental to the success of the *Genetics in the Sertão* program, by continously monitoring the overall health of the population and identifying new disease cases.

Genetic counseling

General information on the effects of a disorder such as MPS VI is initially provided through lectures and workshops conducted at community level, to explain the nature of the disease, and the possible implications of family testing. In families with an affected member multi-generation pedigrees are constructed, subject to the prior approval of family members and on the basis of the information they provide.

Because of the highly endogamous nature of the Monte Santo population, individuals thought to be carriers of the causative ARSB p.H178L mutation in MPS VI often appear in several pedigrees of nuclear families. A blood sample is requested for DNA testing where pedigree analysis suggests that an individual may be at 50% or 25% risk of being a carrier for the p.H178L mutation, along with a sample from his/her partner and any children over 18 years of age. Before such a test is offered its possible implications are again explained, and formal permission to sample is separately obtained from each individual.

Treatment and neonatal screening

In the initial stages of the program, patients with MPS VI had to travel weekly to Salvador, the capital of Bahia, to receive enzyme replacement infusions (ERT) with Galsulfase, the only specific treatment for MPS VI, which necessitated a round trip of 700 km. However, in April 2011 an ERT center for MPS VI was inaugurated at the municipal hospital of Monte Santo,

where local doctors and nurses have been trained in the provision of treatment, with a medical geneticist in regular attendance. As early introduction of therapy seems to provide a better prognosis (McGill et al., 2010), a screening program for MPS VI was recently established for newborns in Monte Santo.

Conclusions

The experience gained in the *Genetics in the Sertão* program has proved invaluable to the population Monte Santo, where in the past severe inherited disorders such as MPS VI were untreatable and represented a major health burden not only to families with affected members but to the community as a whole. In more general terms, *Genetics in the Sertão* has demonstrated the feasibility of establishing such a program in an under-privileged rural population, a lesson which given community support is applicable to other similar communities across Latin America and throughout the developing and middle income world.

Acknowledgements

The authors gratefully acknowledge the financial support provided by INAGEMP - National Institute of Population Medical Genetics (grant CNPq 573993/2008-4), and the Foundation of Research Support of the State of Bahia (FAPESB). Dr. A.X. Acosta was the recipient of a National Council of Technological and Scientific Development (CNPq) Scholarship, held as Visiting Researcher in the Centre for Comparative Genomics, Murdoch University, Australia.

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Table I

Brazil: Demographic and health summary profile 2012

Population	194.3 million
Urban, %	84
Mean income per person	US$11,000
Total fertility rate	1.9
Life expectancy at birth (yr):	
Male	70.3
Female	77.1
Neonatal mortality rate	11/1,000
Infant mortality rate	20/1,000
Under 5 mortality rate	22/1,000
Children <5yr under-weight, %	2
Maternal mortality rate	68.7/100,000
Deaths due to non-communicable diseases, %	74

Sources: Brazil (2011); IBGE (2009, 2010); PRB (2012); UNICEF (2012); WHO (2010, 2011).