Epidemiology of Prenatal Genetic and Environmental Factors of Mental Retardation in Cuba

Araceli Lantigua Cruz, MD, PhD, Miriam Portuondo Sao, MD, MSc, Teresa Collazo Mesa, PhD, Roberto Lardoeyt Ferrer, MD, PhD

ABSTRACT

Introduction One of the most sensitive disabilities in human beings is intellectual disability. In April, 2003, a 10-month study was completed of all persons in Cuba with mental retardation (MR), producing results that included epidemiological variables on a national scale.

Objective Through follow-up research, this paper describes and analyzes 4 prenatal factors associated with MR: Down syndrome (DS), fragile X syndrome (FXS), consanguinity, and maternal alcohol use during pregnancy, in order to provide recommendations for health system decision-makers on consolidating prevention strategies at the community level and improving individual attention to persons with MR.

Materials & Methods All studies were carried out on the basis of strict ethical principles. Data for the 4 prenatal factors was gleaned from the national study’s database. Additional data on affected individuals was obtained through home visits. A previously developed screening instrument was used for clinical genetic analysis to classify possible MR causal factors as prenatal, perinatal, postnatal, psychosis, and unclassifiable. Prenatal included causal factors such as: genetic (by clinical genetic examination, metabolic screening in urine, and routine karyotypes); nonspecific (evidence of prenatal causal factor without diagnosis of genetic or environmental etiology); and environmental (prenatal medical history of biological, physical, or chemical teratogens, endocrine-metabolic diseases, or other maternal diseases known to affect fetal neurodevelopment). Frequency, prevalence, and percentages were reported using a descriptive statistical method. Impact of interventions and actions over time were also compared.

Results MR prevalence in Cuba is 1.25%, lower than the value of 2%-3% reported in developed countries. National prevalence of DS was found to be 4.3 per 10,000 population, representing 22.1% of persons with MR attributed to an ascertained genetic cause. FXS prevalence in a population of individuals of both sexes with MR, initially classified as nonspecific prenatal, psychosis, and unclassifiable, was 2.5 per 1,000 of that population; however, in males of the same population, prevalence was 3.7 per 1,000. At this first stage, such results indicate that this syndrome contributes biologically to the 1.46:1 male/female ratio among the 140,489 individuals with MR. Maternal alcohol use during pregnancy was found in 4.22% of persons with MR and consanguinity was present in 6.89% of the population with MR (10.9% of persons with mild prenatal MR and 14.2% with severe MR). This national data is subdivided by regions and provinces in this paper.

Conclusions Prevalence of MR in Cuba is lower than reference values for developed countries. Knowledge generated by this study about 4 specific causes of MR constitutes pioneering research in the Cuban context, contributing to the field of medical genetics. The results offer the basis for formulation of new scientific contributions related to MR genetics as well as preventive approaches to such genetic factors as consanguinity and to environmental factors such as maternal alcohol use during pregnancy, which affect or target embryo-fetal development of the nervous system.

Keywords: Epidemiology; Mental retardation; Down syndrome; Fragile X syndrome; Consanguinity; Maternal alcohol use; Immunohistochemical test; Molecular genetics; Cytogenetics; Genetic

INTRODUCTION

In the etiology of mental retardation (MR), environmental factors may involve the prenatal, perinatal, or postnatal stages of development, while genome-attributable defects are conceptually prenatal, independent of the neurodevelopmental moment when the cognitive defect manifests. Thus in general, the origins of mental retardation can be classified as prenatal, perinatal, and postnatal.

These causal criteria were put forward by Gustavson et al. in Sweden,[1] who added as an independent category psychoses with mental retardation, describing as unclassifiable those cases with no criteria for discerning their etiology.

A group of researchers in Cuba has worked in this field for over 20 years, incorporating the various factors that may cause or be associated with the appearance of MR.[2,3] In April 2003, a 10-month national study was concluded by the Cuban national health system, revealing an MR prevalence of 1.25% in total population.[3]

Based on the study, the objective of the research for this paper is to describe and analyze 4 prenatal factors with recognized causal association to MR – Down syndrome, fragile X syndrome, consanguinity, and maternal alcohol use during pregnancy – in order to provide recommendations for health system decision-makers on consolidating prevention strategies at the community level and improvement of individual attention to persons with MR.

MATERIALS AND METHODS

Data for analysis of the 4 prenatal factors was gleaned from the national study’s database, protected under the study’s protocol by the National Disabilities Program headquartered at the National Center for Medical Genetics, and to which the principal author has authorized access.[3] After affected individuals were identified, additional data was obtained through home visits made in each community, municipality, and province by Master’s Degree
candidates in the field of Genetic Counseling, and also through specialized evaluations.

The national study, as well as this follow-up study, were carried out on the basis of strict ethical principles, complying with all applicable requirements regarding human subjects set forth in international documents such as the World Medical Association Declaration of Helsinki (as amended, 2004)[4] and the UNESCO Declaration of 2003,[5] including confidentiality of information provided by persons and their families, as well as of the results of blood screenings. Both studies were based on voluntary participation, obtaining informed consent of parents or guardians and assent by intellectually disabled persons (with mild mental retardation, MMR) who participated in the study and including informed consent for karyotype blood analysis or molecular study for detection of the FMR1 mutation.[3,6]

Detailed Methodology
Cognitive disability was determined by teams from Orientation and Diagnostic Centers (CDO), including professionals from various fields (psychologists, specialists in special education, psychometrists, pedagogues, speech therapists) who applied intelligence (IQ) tests and evaluated behavior of persons with suspected mental retardation, assessing degree of MR severity.[7]

A previously developed screening instrument was used for clinical genetic analysis by professionals trained in its use, permitting classification of possible MR causal factors. Working as a team, these professionals classified causal factors as prenatal, perinatal, postnatal, psychosis, and unclassifiable, according to parameters discussed by Gustavson.[1] This instrument was applied by a family physician and a special education specialist. In cases where there were doubts as to classification, patients were visited and examined by clinical geneticists and other specialists as necessary (neurologists, pediatricians, etc.). Furthermore, these individuals received follow-up visits by family medicine specialists or university-level nurses (260 in total throughout the country, in all provinces and municipalities) as part of their Genetic Counseling Master’s research (with 4th-, 5th- and 6th-year medical students, academic year 2004-2005).

The group classified as prenatal included the following causal factors:

- Genetic: by clinical genetic examination, metabolic screening in urine, routine karyotypes. Diagnosis of genetic conditions and etiology of congenital defects previously carried out in clinical genetics services were taken into consideration.
- Nonspecific: evidence of prenatal causal factor without diagnosis of genetic or environmental etiology.
- Environmental: prenatal medical history of biological, physical, or chemical teratogens, endocrine-metabolic diseases, or other maternal diseases known to affect fetal neurodevelopment.

Cases were classified as perinatal and postnatal when a history of environmental factors such as perinatal injury, infection, intoxication, or accidents could explain the cause of MR, provided there was no evidence of prenatal damage. Persons were considered unclassifiable who presented with nonsyn-

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To define maternal alcohol use during pregnancy as a possible cause of MR, persons with this history but who presented other known genetic syndromes were excluded. Maternal alcohol use was considered only in cases of persons with this history who presented a dysmorphic constellation characteristic of fetal alcohol syndrome (FAS), or who manifested nonsyndromic MR with this prenatal history.[12]

Frequency, prevalence, and percentages were reported using a descriptive statistical method.[13] Impact of interventions and actions through time were also compared.

Taking into consideration population density, the country was divided into the following regions for data analysis:

**Western region:** Pinar del Río, Havana, Havana City, and Matanzas provinces, plus the special municipality Isla de la Juventud (Isle of Youth).

**Central region:** Cienfuegos, Villa Clara, Sancti Spíritus, Ciego de Ávila, and Camagüey provinces.

**Eastern region:** Las Tunas, Holguín, Granma, Santiago de Cuba, and Guantánamo provinces.

**RESULTS**

In the national study 140,489 individuals with intellectual disability were detected. Of these, 79,442 presented mild mental retardation (MMR) and 61,047 severe mental retardation (SMR). Global prevalence of MR is 1.25%.[3]

Figure 1 shows global prevalence of MR increasing towards highest values in the eastern region, as is the case with MMR.

In Table 1, results for MR in males and females are illustrated according to age, severity, and selected causes. It should be noted that males presented more frequently in the MMR group, as well as in the SMR group, although in the latter differences are smaller and more homogeneous.

**Down Syndrome**

4,919 individuals with Down syndrome were detected nationally for a prevalence of 4.3 per 10,000 population. Table 2 shows DS prevalence by province as per 10,000 population, and weight of DS as percent of all persons with MR, and as percent of MR cases of genetic origin.

Figure 2 shows declining DS prevalence with increasing age. The map in Figure 3 illustrates DS prevalence (per 10,000 population) in total population by region, as well as its distribution by age group (0-4 years and 5-14 years) and region. Differences can be observed, with slightly higher prevalence in total population in the western region and variable prevalence by age group.

The national screening studied 414 DS cases, and an additional 142 cases, which were previously studied by clinical geneticists or through institutional research,[2] for a total of 556 DS persons. Although there are a larger number of DS patients with karyotypes, these were not included in our results here since they were not available at the time research for this paper was carried out. The originating phenomena were distributed as follows: 513 due to trisomy 21 (92.0%); 21 D/21 or G/21 to translocation (3.8%), and 22 to mosaicism (3.9%).

**Fragile X Syndrome**

Of the 658 males screened by immunohistochemical test in Havana City province, 61 males in 24 families presented full mutation of the FMR1 gene. In the rest of the country, af-
ter clinical examination based on the established scoring, molecular studies of 245 males revealed another 86 mutations. Thus, of those presenting MR nationally, a total of 147 males manifested fragile X syndrome with full mutation of FMR1 gene, and 21 heterozygotic females were detected with full mutation. Molecular study was indicated in 81 women who manifested MR and were related to men with a high clinical score for FXS.

FXS thus presents a prevalence of 2.5 per 1,000 in 66,794 MR persons of both sexes in Cuba whose origins were classified as prenatal, psychosis, and unclassifiable. Prevalence is 3.7 per 1,000 for males in that group (39,332). This population of MR individuals was selected because in these groups it was possible to detect the clinical characteristics required for scoring as defined by De Vries[10] (craniofacial dysmorphism, autism, first-degree family antecedents with criteria of segregation for this dynamic mutation, macro-orchidism, etc.).

In the male population with general MR, excluding those of perinatal and postnatal etiology (50,381), FXS represented a prevalence of 2.9 per 1,000. Figure 4 shows results for this population by region. Greatest prevalence was registered in the central Cuban provinces, especially Cienfuegos, where frequency was 5.5 per 1,000 related to general MR population (excluding perinatal and postnatal).

Consanguinity
Consanguinity was present in 5.87% of all MR cases and in 11.98% of MR cases of prenatal etiology. However, interesting differences, which surpass the national frequency, were observed in several provinces, as seen in Table 3.

Of the 69,489 individuals with MMR (nationally, excluding Havana City and Sancti Spíritus provinces), 4,470 were offspring of consanguineous parents; of the 51,595 with SMR (excluding the same provinces), consanguinity was present in 3,976. In both, the kinship between parents was mainly first cousins; other kinships were those between more distant cousins or between uncles and nieces or aunts and nephews.

Figure 5 shows frequency of consanguinity for MR in total population by region, excluding Havana City and Sancti Spíritus provinces.

Alcohol in Etiology of MR
A history of alcohol use during pregnancy was described in cases of 5,934 individuals with varying severity of MR. Of those, dysmorphic evidence by physical examination was detected in 1,408, while this history was also present in 3,760 indi-

Table 2: Prevalence of Down Syndrome (DS) by Province, Cuba

<table>
<thead>
<tr>
<th>Province</th>
<th>DS prevalence in total population (per 10,000)</th>
<th>DS in persons with MR (%)</th>
<th>DS in genetic-origin MR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinar del Río</td>
<td>5.4</td>
<td>3.54</td>
<td>13.11</td>
</tr>
<tr>
<td>Havana Province</td>
<td>4.7</td>
<td>4.05</td>
<td>20.60</td>
</tr>
<tr>
<td>Havana City</td>
<td>4.4</td>
<td>6.94</td>
<td>58.38</td>
</tr>
<tr>
<td>Matanzas</td>
<td>4.4</td>
<td>4.05</td>
<td>21.48</td>
</tr>
<tr>
<td>Isle of Youth</td>
<td>4.1</td>
<td>3.91</td>
<td>17.82</td>
</tr>
<tr>
<td>Cienfuegos</td>
<td>4.0</td>
<td>3.06</td>
<td>19.00</td>
</tr>
<tr>
<td>Villa Clara</td>
<td>4.6</td>
<td>3.48</td>
<td>15.37</td>
</tr>
<tr>
<td>Sancti Spíritus</td>
<td>3.6</td>
<td>3.09</td>
<td>41.18</td>
</tr>
<tr>
<td>Ciego de Ávila</td>
<td>4.8</td>
<td>3.30</td>
<td>20.30</td>
</tr>
<tr>
<td>Camagüey</td>
<td>4.1</td>
<td>2.83</td>
<td>23.67</td>
</tr>
<tr>
<td>Las Tunas</td>
<td>3.3</td>
<td>2.47</td>
<td>32.35</td>
</tr>
<tr>
<td>Holguín</td>
<td>4.0</td>
<td>2.49</td>
<td>19.32</td>
</tr>
<tr>
<td>Granma</td>
<td>4.3</td>
<td>3.59</td>
<td>24.52</td>
</tr>
<tr>
<td>Santiago de Cuba</td>
<td>4.3</td>
<td>2.60</td>
<td>17.44</td>
</tr>
<tr>
<td>Guantánamo</td>
<td>4.8</td>
<td>2.89</td>
<td>16.02</td>
</tr>
<tr>
<td>Total</td>
<td>4.3</td>
<td>3.50</td>
<td>22.07</td>
</tr>
</tbody>
</table>

*n=140,489
Source: Analysis of results obtained from the National Study of Disabilities and Persons with Mental Retardation in Cuba, National Medical Genetics Center, Havana, 2003.
individuals with MR who showed no dysmorphic characteristics. The typical dysmorphic features of Fetal Alcohol Syndrome (FAS) were not clearly identified in 766 individuals.

Table 4 shows maternal alcohol use during pregnancy (MAP) associated with MR in the general population of persons with MR, and in persons with MR due to prenatal causes. Percentages presenting dysmorphic features or nonsyndromic MR are also shown.

Figure 6 represents maternal alcohol use in pregnancy associated with MR in Cuba, indicating the problem is more serious in the eastern region. As shown in Table 4, Havana City and Matanzas provinces stand out in the western region. In the central region, which has the lowest frequency of alcohol use associated with MR, Camagüey stands out with the highest alcohol use. Notice that from this province on, frequencies are high in the provinces of the eastern region, especially in Santiago de Cuba.

DISCUSSION
The prevalence of MR nationally is 1.25%, lower than reference values for developed countries, reported between 2%-3%.14 However, there are important regional differences that may be related to geographical and socio-cultural characteristics—both in the case of regions with lower prevalence, such as Havana City and Holguín, and with higher prevalence, such as Santiago de Cuba and Guantánamo.3 This aspect merits further study by researchers.

Down Syndrome (DS) and Fragile X Syndrome (FXS)
These two syndromes are analyzed in detail in our country, since they are reported as the most frequent genetic causes of MR worldwide.14

DS is the most frequent genetic cause of mental retardation. Its clinical diagnosis at any age is unequivocal for the majority of specialists working in the care of these persons. In our research, the clinical-genetic study of persons with mental retardation was carried out by specialists in clinical genetics who were present throughout the research. DS was 22.10% of the diagnoses of mental retardation of genetic etiology. Provinces such as Havana City, Sancti Spíritus, and Las Tunas exhibit the highest percentages of DS as a genetic cause of MR (Table 2). Variations found may be due to several reasons, mortality among them. 3,008 DS cases in all of Cuba were older than 20 years (61.3%); Havana City province makes up 20.2% of this population. In turn, this was the province with more DS patients older than 60. 72 persons with DS in Cuba are older than 60, 1.5% of all persons with DS. From the age of 20 forward, prevalence of DS decreases, as shown in Figure 2.

The DS life chart, put forward by Baird and Sadovnick,15 establishes that 85% of DS babies survive the first year of life; 80% survive 10 years, and 50% live more than 20 years. Our results in relation to this life chart deserve a more detailed analysis which goes beyond the objectives of this paper, but they generate questions and hypotheses for further study.

Prevalence values are quite homogeneous in the three regions of the country. However, these differ for the populations aged 0-4 years and 5-14 years in the three regions (Fig.3). Low prevalence can be seen in the 0-4 year-old population in the west, and high prevalence in the central and mid-eastern regions.

We cannot explain these differences with certainty, but they may be due to at least two reasons: greater coverage of the program for prenatal detection of DS in the last 6 years in Havana City (which may lead to fewer births with DS), and/or lower mortality.

Table 3: Consanguinity in Mental Retardation (MR): By Province for Total MR Population and for MR Population of Prenatal Cause According to Severity (MMR or SMR)

<table>
<thead>
<tr>
<th>Province</th>
<th>% Consanguinity in MR Population*</th>
<th>% Consanguinity in MR of Prenatal Cause Total</th>
<th>% Consanguinity in MR of Prenatal Cause MMR</th>
<th>% Consanguinity in MR of Prenatal Cause SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinar del Río</td>
<td>8.54</td>
<td>18.23</td>
<td>18.32</td>
<td>21.79</td>
</tr>
<tr>
<td>Havana Province</td>
<td>5.00</td>
<td>10.21</td>
<td>4.48</td>
<td>11.87</td>
</tr>
<tr>
<td>Havana City</td>
<td>**</td>
<td>**</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Matanzas</td>
<td>5.59</td>
<td>11.56</td>
<td>10.36</td>
<td>12.86</td>
</tr>
<tr>
<td>Isle of Youth</td>
<td>5.97</td>
<td>9.87</td>
<td>5.33</td>
<td>7.71</td>
</tr>
<tr>
<td>Villa Clara</td>
<td>6.44</td>
<td>13.27</td>
<td>12.04</td>
<td>15.07</td>
</tr>
<tr>
<td>Cienfuegos</td>
<td>5.96</td>
<td>12.89</td>
<td>9.15</td>
<td>9.26</td>
</tr>
<tr>
<td>Sancti Spíritus</td>
<td>**</td>
<td>**</td>
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<td>**</td>
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<tr>
<td>Ciego de Ávila</td>
<td>6.56</td>
<td>13.50</td>
<td>9.48</td>
<td>21.17</td>
</tr>
<tr>
<td>Camagüey</td>
<td>7.38</td>
<td>17.30</td>
<td>6.55</td>
<td>8.52</td>
</tr>
<tr>
<td>Las Tunas</td>
<td>12.36</td>
<td>28.07</td>
<td>13.16</td>
<td>16.30</td>
</tr>
<tr>
<td>Holguin</td>
<td>10.29</td>
<td>23.43</td>
<td>32.70</td>
<td>35.59</td>
</tr>
<tr>
<td>Granma</td>
<td>9.69</td>
<td>**</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Santiago de Cuba</td>
<td>5.43</td>
<td>10.52</td>
<td>5.18</td>
<td>5.74</td>
</tr>
<tr>
<td>Guantánamo</td>
<td>7.21</td>
<td>14.83</td>
<td>36.70</td>
<td>38.00</td>
</tr>
<tr>
<td>TOTAL</td>
<td>6.89</td>
<td>11.98</td>
<td>10.91</td>
<td>14.19</td>
</tr>
</tbody>
</table>

*n=121,084 excluding Havana City and Sancti Spíritus provinces. Havana City and Sancti Spíritus provinces are still pending in this study, and Granma province shows global values but with no specificity for MR due to prenatal causes.

Source: Analysis of results obtained from the National Study of Disabilities and Persons with Mental Retardation in Cuba, National Medical Genetics Center, Havana, 2003.
Higher prevalence of MR in males has been observed historically in research involving populations with this disability.[19] In Cuba, a male(M)-female(F) ratio of 1:1 was registered in the last census.[20] However, in our study of 140,489 subjects with MR, this ratio was 1.46M:1F; and in a study of 512 Cuban patients institutionalized due to SMR caused by prenatal and unclassifiable factors, the ratio was 1.5M:1F.[2] In Table 1, this marked male predominance is observed in persons with MMR classified as prenatal, psychosis, and unclassifiable; this is quite marked in the group aged <15 years among SMR cases.

Such differences had initially been attributed to various factors,[16] but advances in human genetics have now revealed that the X-chromosome carries a constellation of genes whose mutations are linked to MR.[21] The genotypic hemizygotic state of males may thus explain that a simple mutation – even recessive – may be biologically expressed, both in severe forms (even in complex syndromes) and in nonsyndromic forms of mental retardation.[22] The literature reports an MMR ratio as high as 1.9M:1F;[22] and 50% of all MMR forms have been attributed to X-linked mutations.[21] At least 885 proteins expressed in the brain have also been identified, 40% of which have their genes in the X-chromosome.[22] This may explain the excess of males with MR of different degrees, especially in unclassifiable MR after genetic examination, based on the absence of family and prenatal history or dysmorphisms. Such mutations may be expressing for the first time in a male individual.

Fragile X syndrome is the second genetic cause of mental retardation after Down syndrome,[14] and the first genetic cause determined by a mutation with Mendelian inheritance linked to the X-chromosome.[22] Unlike Down syndrome, the clinical diagnosis has its peculiarities. The phenotype may be easily recognized or suspected in the post-pubescent period by the presence of macroorchidism, but it is difficult to identify in childhood and its detection by dysmorphological and neurological indicators after birth is not possible.[23-25]

FXS prevalence in males has varied according to population studied and diagnostic methods used. In Nova Scotia, for instance, a serious epidemiological study found no evidence of this mutation in the screened population.[26] In other populations, values have been reported from 1 per 1,000 population to, more recently,
An interesting phenomenon involved in the genetics of mental retardation is the detection of affected persons whose parents were consanguineous partners. The general frequency of this risk indicator observed in individuals with mild mental retardation explains the polygenic or multifactorial character of 10.91% of those with MR and 14.19% for the most severe forms of MR (Table 3). This denotes the possibility that other types of birth defects are involved, due to the high probability in marriages at risk for being heterozygotic for uncommon simple mutations that are only expressed in homozygotic persons, such as the specific metabolic defects of genetic syndromes with autosomal recessive inheritance.[30]

In one of the municipalities with the highest MR prevalence, Urbano Noris in Holguín province, high frequencies of consanguinity were also confirmed in persons with MMR and SMR. In this community, marriage between first cousins was so common that there was a frequency of 10.3% consanguinity in the Estrada area of town when the study was conducted. There are only 3 surnames in this community, and an MR rate of 10%. Results of educational work concerning the risks of these marriages for their offspring may be changing couples’ attitudes in this regard. In Estrada in 2003, 57.1% of pregnancies were the result of consanguineous marriages. In 2004, there was a reduction in this phenomenon among expectant mothers (29.4%), whereas in 2005, no history of consanguinity was found in the 14 pregnant women of this community.[31]

In Caimito in Havana Province, with a population of 34,672 and an MR prevalence of 0.68%, it was found that consanguinity explained the presence of nonsyndromic MMR in 11.8% of people with MMR, and in 9.7% of the syndromic forms with SMR.[32]

The frequency of consanguinity in parents of persons with MR is a changing phenomenon that varies in each country, and depends on the geographical characteristics and customs of the population.[33] In a study on consanguinity and MR in India, 160 (30.94%) of 517 people studied were born from consanguineous marriages.[34]

In Cuba, consanguinity has been observed as a variable cause of MR. The highest values of consanguinity occur in the eastern region (Las Tunas, Holguín, Granma, and Guantánamo provinces, in that order), whereas in the western provinces, Pinar del Río showed the greatest frequency of this indicator (Table 3).

**Maternal Alcoholic Consumption as a Cause of MR**

Another etiological prenatal factor for MR was alcohol consumption during pregnancy. In 5,934 persons with mental retardation, declaration of alcohol use during the whole pregnancy or part of it was the only prenatal antecedent for MR. Of these, 21.9% (Table 4) also showed dysmorphic signs that characterize fetal alcohol syndrome (FAS),[12] and in the rest the “hadegen” effect[35] of this common chemical teratogen was observed.

The clinical-genetic study undertaken in the country revealed provinces and municipalities more accustomed than others to consuming alcoholic beverages during pregnancy (Figure 6). In the eastern region, the highest values were detected in Santiago de Cuba, Guantánamo, and Holguín. Some of these, like Holguín, also coincide with the high consanguinity rate as a causal factor of MR.

In the Estrada community, a reduction of alcohol consumption during pregnancy has been observed in the last few years, from 72.2% in 2003 to 14.3% in 2005.[31] This behavioral change, the same as in consanguinity, can be attributed to reinforced educational efforts by trained professionals as a result of the national study.

**CONCLUSIONS**

The prevalence of MR in Cuba is lower than referenced values for developed countries. In this article, we provide original epidemiological data from clinical-genetic research in Cuba on 4 specific causal factors of MR, which we hope will contribute to new hypotheses for the study of the genetics of mental retardation and the environmental factors affecting embryo-fetal neurological development. Linking this new knowledge to diagnosis, treatment, and prevention of genetic disorders and birth defects, respecting bioethical principles, can lead to improved quality of life, as shown by some of the data mentioned in the discussion.

We hope that our findings will add to the knowledge base in Cuba for health professionals trained as specialists in medical genetics and genetic counseling as they carry out important educational activities at the national and community level, and for the National Network of Medical Genetics. In particular, it is hoped that public education on consanguinity and alcohol use during pregnancy will have positive effects on prenatal risk factors for MR.

Analysis of data for the 2 most frequent genetic causes of MR serves to inform public health authorities and decision-makers as they implement measures to improve prenatal detection of DS and to provide information to families with persons affected by
FXS. The design of preventive strategies based on the technical and ethical foundations of genetic counseling is an expected benefit. At the same time, the epidemiological data point to the need for continued research focusing on the epidemiological and molecular characteristics of FXS in the Cuban population.

We concur with Byers who, when referring to genetic language applied to medical genetics and its ethical principles said, “if only we spoke the same language, we would have so much to discuss.”[36] We would add that speaking the same language would improve the population’s quality of life.

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30. Araceli Lantigua Cruz (Corresponding Author), Full Professor, Higher Institute of Medical Sciences of Havana. Clinical Genetics Specialist. Vice Director for Teaching, National Medical Genetics Center, Havana, Cuba. lantigua@in-omed.sld.cu

31. Teresa Collazo Mesa, Associate Researcher and Head, Molecular Genetics Laboratory, National Medical Genetics Center, Havana, Cuba.

32. Roberto Lardoeyt Ferrer, Instructor, Higher Institute of Medical Sciences of Havana. Clinical Genetics Specialist, National Medical Genetics Center, Havana, Cuba.

ACKNOWLEDGEMENTS

This national study could not have been carried out without the support of the Cuban government, its support of Medical Genetics, and economic and organizational support from the Ministry of Public Health. We would also like to thank the Clinical Genetics specialists, the Master’s Degree candidates in Genetic Assessment, and other researchers, technicians, and specialists of the National Medical Genetics Center, the 14 Provincial Medical Genetics Centers and 169 Municipal Centers, all part of the National Medical Genetics Network, who bring preventative and clinical care to the disabled and their families in Cuba.