Brazilian Journal of Genetics, 18, 3, 451-457 (1995)
(Revista Brasileira de Genética)

Genetic and congenital diseases in a Mexican Pediatric Hospital

P. Barros-Nuñez and C. Medina

ABSTRACT

A survey of patients with genetic and/or congenital diseases (GCD) in a tertiary care pediatric hospital of Guadalajara-Mexico was undertaken, in order to determine the hospitalization frequencies and duration.
Of all admissions, 40% had genetic and/or congenital disorders. This total frequency is similar to those reported in some other surveys; however, its distribution into etiological groups showed interesting differences. The patients with GCD required significantly more lengthy hospitalization, more surgeries and more laboratory studies. Likewise, this kind of patient had a statistically higher mortality rate than other patients. Most of the patients came from the metropolitan area of Guadalajara.

INTRODUCTION

Although knowledge of the frequency of genetic and/or congenital diseases (GCD), occurring in different populations, is a fundamental objective of medical genetics (OPS, 1984; Jiménez-Balderas *et al.*, 1985; Mutchinick *et al.*, 1988), it is also important to determine the economic and administrative burden of GCD on health services. Few systematic studies have been made with these purposes in mind (Barreiro *et al.*, 1976; Hall *et al.*, 1978; Penchaszadeh, 1979; Carnevale *et al.*, 1985; Carnevale, 1986).

In the majority of the Latin American countries, GCD have not received enough attention from the public health services, which is partly explained because health problems due to environmental and socioeconomic causes are responsible for most of the morbidity-mortality in childhood. On the other hand, poor statistical information about GCD has supported the disputable idea that these disorders are irrelevant (Castilla *et al.*, 1974; OPS, 1984).

Certainly, information on the magnitude and burden of GCD in developing countries is fragmentary; however, some studies show that their incidences are similar to those observed in developed countries. From this premise, it is accepted that around five percent of births in our region have developing abnormalities due to genetic factors. Moreover, when the common disorders of adult life (chronic and degenerative diseases) are added, the corresponding proportion will rise to 10 percent (OPS, 1984; Carnevale, 1986).

Congenital disorders are included among the ten most important causes of childhood mortality in Latin America (2-29%. OPS, 1984). In Mexico, Armendares *et al.* (1974) found that 29.5% of deaths in a pediatric hospital were, wholly or partly, due to genetic causes. On the other hand, GCD account for 10 to 25% of the admissions in the tertiary care centers in our region (OPS, 1984). Interestingly, in Latin America (as in developed countries), the relative importance of GCD, as a cause of hospitalization or death, is greater when morbidity and mortality rates are lower (Penchaszadeh, 1979).

Division de Genetica, Centro de Investigacion Biomedica, Centro Medico de Occidente, Instituto Mexicano del Seguro Social, Sierra Mojada 800. AP. 13838. Guadalajara Jal. Mexico. Phone: (3352) 617-0060, Fax: (52-3) 618-1756. Send correspondence to P.B.-N.

MATERIAL AND METHODS

This study was conducted at the Pediatric Hospital of the "Centro Médico de Occidente" of the "Instituto Mexicano del Seguro Social" (IMSS), Guadalajara. It is a 269-bed, tertiary care hospital with an annual average (last three years) of 10,210 admissions and 69,090 outpatients. This hospital offers four hours/day of clinical genetics service to four first-time and eight subsequent outpatients. In addition, there is a consultation system for the hospitalized patients.

The universe was the IMSS insured population, under 16 years of age, residing in the states of Jalisco, Baja California Norte, Baja California Sur, Sonora, Sinaloa, Nayarit, Aguas Calientes, Michoacan, Colima and Guanajuato. Among these, 3% (89,595 patients) were sent to a tertiary care hospital (potential population calculated by the IMSS).

The following information was recorded and analyzed:

a) The discharge sheets and medical records of the hospitalized patients between January and October of 1992 gave: affiliation number, age, sex, origin, length of hospitalization, final diagnosis, surgeries and consultation to the genetic service. In addition, the hospital deaths occurring in the same period and having a GCD as a primary or secondary cause were recorded.

These patients were assigned to the following etiological categories:

1. Clearly genetic disorders.
   a) Autosomal dominant.
   b) Autosomal recessive.
   c) X-linked.
   d) Chromosomal.

2. Multifactorial conditions.

3. Familiar disorders.

4. Developmental anomalies.
   a) Unknown etiology.
   b) Known etiology.

b) From the medical records of the first-time genetic outpatients in the same period: affiliation number, age, sex, origin, diagnosis, number of subsequent appointments to genetic and other services and, number of laboratory studies. These patients were assigned to the same etiological categories, including three others:

5. Nongenetic disorders.

6. Normal individuals.

7. No diagnosis.

Because of the genetic heterogeneity of many of these disorders, the assignation was done rigorously according to the established diagnosis in the records.

Statistical analysis by means of a chi-square test were made for: age and sex, surgeries and deaths. A Mantel-Haenszel test was applied for the laboratory requirements analysis, and a Z test for length of hospitalization.

RESULTS AND DISCUSSION

The Pediatric Hospital of the Centro Medico de Occidente receives referrals of difficult and complex disorders from first and second level hospitals. The frequency of GCD in the different hospitals shows wide variations, depending probably on the condition and location of each one (Hall *et al.*, 1978); therefore, the reported frequencies in this paper could be representative only for third level hospitals in Mexico and probably in Latin America. On the other hand, we previously knew that an important proportion of physical and mental disorders such as mental retardation, deafness, blindness and locomotor abnormalities, affecting at least 11% of the Latin America population (OPS, 1984), would be only partly included in our study.

Appendix 1 and 2 shown the main specific diagnoses found among in and outpatients respectively.

a) Frequency of GCD

Among the 8,387 admissions occurring from January to October, 40.6% had a GCD as primary or secondary diagnosis. About one-half of these patients had a disorder considered of multifactorial etiology and only 12.8% of Mendelian or chromosomal etiology (Table I).

Of 434 first-time consulting outpatients, 92% had a GCD; more than one third of these were of clear genetic etiology and almost one half had chromosomal abnormalities. Multifactorial and familiar disorders were found in two fifths of the outpatients with GCD (Table II).

Table I - Frequency distribution of the 8,387 impatients according to etiology.

Categories	% GCD
1. Genetic	
a) Autosomal dominant	3.5
b) Autosomal recessive	4.8
c) X-linked	1.8
d) Chromosomal	2.7
2. Multifactorials	
- Cardiovascular	16.6
- Cleft lip-palate	7.7
- Neural tube defect	3.3
3. Familial aggregation	20.5
4. Developmental anomalies	
a) Unknown cause	21.0
b) Known cause	0.5
5. Non genetic	59.3

GCD - Genetic and congenital diseases.

Table II - Frequency distribution of the 434 outpatients according to etiology.

Categories	% Group	% Total
1. Genetic		32.7
a) Autosomal dominant	29.6	
b) Autosomal recessive	21.1	
c) X-linked	2.8	
d) Chromosomal	46.4	
2. Multifactorial		20.5
3. Familial aggregation		1.4
4. Developmental anomalies		17.7
a) Unknown cause	94.8	
- Single abnormalities	84.9	
- Syndromes	15.1	
b) Known cause	5.2	
5. Undiagnosed		
6. Without GCD		
7. Healthy individuals		6.4

The clearly genetic disorders (chromosomal and single gene) were much more frequent among outpatients than among inpatients, and vice-versa for multifactorial and developmental abnormalities. This last is probably explained because many of these patients were admitted and studied only for a specific or main abnormality (eg. cardiopathy) without considering the complete clinical syndrome (eg. Turner syndrome).

Interestingly, during the study, only 10.6% of the inpatients with GCD consulted the genetic service for a specialized evaluation. The total frequency of patients with GCD in our study is intermediate between those occurring in developed and undeveloped countries (Table III).

Table III - Frequency of genetic disease among different Pediatric Hospitals (% total admissions)

	Single gene	Chromosomal	Multifactorial	Developmental anomalies	Nongenetic
Hall J. (1978) Seattle. WA. USA	3.9	0.6	22.1	13.6	46.6
Penchaszadeh V. (1979) Caracas. Venezuela	3.2	0.7	3.3	2.9	89.8
Carnevale A. (1985) México city. México	3.4	1.1	33.8	13.8	48.4
Present study (1992) Guadalajara. México	4.1	1.1	18.4	8.8	59.3

b) Age and sex (Table IV)

Forty percent of the inpatients were in the 1-5 year group, which was twice greater than the -1 year group. This could be due to the large number of tumors and leukemias diagnosed and included in this age group. The frequency distribution between age groups showed statistical differences ($\chi^2_{(3)} = 418.5$; $p \leq 0.001$).

Table IV - Distribution of the 3,406 GCD inpatients according to age and sex.

Age groups	Sex	
	% M	% F
- 1	12.8	9.3
1 - 5	23.0	16.9
6 - 10	11.6	8.5
11 - 15	9.3	5.9
+ 16	1.4	1.1
Total	58.2	41.8

Among the outpatients, more than one third were within the first year of age (39.4%); there was also a statistical difference between the age groups (1-5, 6-10 and 11-15) ($\chi^2_{(3)} = 51.38$; $p \leq 0.001$).

There were more males than females in each group (in and outpatients) with a male/female total ratio of 1.36. ($\chi^2_{(1)} = 92.07$; $p \leq 0.001$).

c) Surgeries and length of hospitalization

On average, 90% of the patients with GCD and only 43% of the patients without GCD required a surgery or a procedure in the operating room ($\chi^2_{(1)} = 1,949.7$; $p \leq 0.001$). Obviously many patients had more than one surgery each.

Patients with GCD were hospitalized an average of 6.92 days each, whereas patients without GCD only 5.45 days ($Z = 16.5$; $p \leq 0.001$).

d) Deaths

Four hundred-seventy-three inpatients died during the period analyzed. Among these 51.5% had a GCD as primary or secondary cause. The mortality rate among inpatients without GCD was significantly lower than among inpatients with GCD (4.6% vs. 7.1%) ($\chi^2_{(1)} = 24.08$; $p \leq 0.001$). The mortality rate in this hospital (5.64%) showed an intermediate position between developed and undeveloped countries.

e) Origin and attendance (Table V)

Among 517 outpatients with a genetic appointment, only 84% attended the service. Nearly 75% of all the patients came from the state of Jalisco and 75% of these were from the metropolitan area of Guadalajara. Apparently, the attendance proportion of foreign patients was in relation to the distance from the hospital.

Table V - Distribution of the patients according to origin.

Origin	%
Guadalajara (mt.a.)	55.9
Jalisco (outside mt.a.)	18.5
Other States	25.5

mt.a.: metropolitan area.

f) Time used in genetic consultation

10,280 first time outpatients were attended by 78 specialized physicians from January to October; a mean 2,358 of physician hours each month. Among all the outpatients (4.22%) had a GCD, however, they received 3.83% of the total of physician hours/month (880 h/p/m).

The 434 first-time genetic outpatients generated 985 subsequent appointments for this speciality (3.26 on average), and 669 more for other specialities. A total of 2,088 consultations was required (4.81 on average).

Considering the time for a complete consultation, we infer that each genetic patient received a total of 64.05 minutes. This time includes administrative registry, anamnesis, physical examination, diagnosis and genetic counseling. Although we were only able to use Bernhardt's parameter, apparently our outpatients did not have enough time in consultation and, probably genetic counseling was the most affected area (Bernhardt and Pyeritz, 1989).

g) Laboratory requirements (Table VI)

Each genetic outpatient required 3.46 laboratory analyses in comparison with 2.28 required by nongenetic patients (Mantel-Haenszel = 43.09; $p \leq 0.001$). A statistical difference was also observed for Rx. (Mantel-Haenszel = 15.73; $p \leq 0.001$) but not for ECG and EEG.

Table VI - Laboratory requirements for outpatients

	Lab. tests	Other tests		
		Rx	ECG	EEG
Genetic patients				
- Patients	317	114	79	32
- Average tests/patients	3.46	2.2	1.3	1
Other patients				
- Patients	50,442	7,354	917	745
- Average tests/patient	2.28	1.4	1.21	1.04

RESUMO

Foi feita uma investigação de pacientes com doenças genéticas e/ou congênitas (GCD) do hospital pediátrico de Guadalajara, México, para determinar a freqüência de hospitalização e duração da mesma.

Quarenta por cento dos pacientes internados tinham uma disordem genética e/ou congênita. Esta freqüência é similar às registradas em outros levantamentos, entretanto a distribuição em grupos etiológicos mostraram diferenças interessantes. Os pacientes com GCD necessitaram de maior tempo de hospitalização, mais cirurgias e estudos de laboratório. Este tipo de paciente teve uma taxa de mortalidade estatisticamente maior que outros pacientes. A maioria dos pacientes vieram de áreas metropolitanas de Guadalajara.

APPENDIX 1

Main specific diagnoses by etiology: inpatients

Autosomal dominant:	No.
Wilms tumor	32
Retinoblastoma	26
Neurofibromatosis	12
Achondroplasia	8
Noonan syndrome	7
Spondyloepiphiseal dysplasia	4
Spherocitosis	4
Osteogenesis imperfecta	4
Tuberous sclerosis	3
Multiple exostoses	3
Marfan disease	2
Others	16
Autosomal recessive:	
Cystic fibrosis	25
Congenital glaucoma	24
Congenital adrenal hyperplasia	17
Sickle cell anemia	16
Cong. cataract	14
Microcephaly	11
Glucogenosis	9
Spinal muscular atrophy	7
Hypophosphatemic rickets	6
Fanconi anemia syndrome	5
Mucopolysaccharidosis	5
Craneostenosis	4
Diastrophic dwarfism	2
Others	19
X-linked:	
Hemophilia A	43
Hemophilia B	8
West syndrome	6
G6PD deficiency	4
Chromosomal:	
Down syndrome	72
Turner syndrome	14
Others	5
Multifactorial:	
Cong. cardiovascular malform.	564
Cleft lip and/or palate	261
Neural tube defect	113
Congenital hip dislocation	89
Club foot	83
Seizures	61
Pyloric stenosis	57
Asthma	55
Hydrocephalus	53
Mat-fetal incompatibility	48
Diabetes mellitus	38
Gastrosquisis	18
Hirschprung disease	11
Congenital anophtalmos	9
Others	118
Familial aggregation:	
Solid tumors	420
Leukemias	225
Lupus erythematosus	14
Renal malformations	10
Others	30
Developmental abnormalities:	
a) *Unknown cause*	
- Single defect	
- Head and neck	225

- Gastointestinal	98
- Genitourinary	220
- Skeletal	99
- Others	54
- Syndromes	22
b) *Known cause*	16
Cong. cardiovascular malf.	5
Others	14
Familial aggregation:	6
Developmental anomalies:	
a) *Unknown cause*	
- Single defect	
- Head and neck	19
- Genitourinary	15
- Skeletal	28
- Syndromes	
- Moebius	2
- Cornelia de Lange	2
- Goldenhar	2
- Others	5
b) *Known cause*	
- Amniotic bands	4
Nongenetic cause:	6
Normal individuals:	28
Undiagnosed	86

APPENDIX 2

Main specific diagnoses by etiology: outpatients

Autosomal dominant	No.
Noonan syndrome	5
Ectrodactyly	3
Osteogenesis imperfecta	3
Ehlers Danlos syndrome	3
Neurofibromatosis	3
Rieger syndrome	2
Retinoblastoma	2
Multiple exostoses	2
Marfan syndrome	2
Hypochondroplasia	2
Others	15
Autosomal recessive:	
Congenital cataract	5
Cong. adrenal hyperplasia	4
Congenital glaucoma	4
Neurosensorial deafness	2
Microcephaly	2
Glucogenosis	2
Others	11
X-linked:	
Duchenne muscular dystrophy	2
Hemophilia A	1
West syndrome	1
Chromosomal:	
Down syndrome	45
Turner syndrome	13
Others	8
Multifactorial:	
Cleft lip and/or palate	35
Psichomotor retardation	15
Neural tube defect	9
Seizures	6
Congenital hip dislocation	5

REFERENCES

Armendares, S., Cortez, R. and **De La Rosa, L.** (1974). El componente genético en la mortalidad infantil. *Rev. Inv. Clin. 26*: 3-18.

Barreiro, C.Z., Negrotti, T. and **Penchaszadeth, V.B.** (1976). Prevalence of genetic disease in a reference pediatric hospital. *Vth International Congress of Human Genetics*, Mexico, 1976. *Excerpts. Med. Intl. Congr. Series. 397*: 60.

Bernhardt, B.A. and **Pyeritz, R.E.** (1989). The economics of clinical genetics services. III. Cognitive genetics services are not self-supporting. *Am. J. Hum. Genet. 44*: 288-293.

Carnevale, A. (1986). Aportaciones de un servicio de genética al estudio de los pacientes de un hospital pediátrico. *Gaceta Médica de México 122*: 5-6.

Carnevale, A., Hernandez, M., Reyes-Miranda, R. and **Paz Camacho, F.** (1985). The frequency and economic burden of genetic disease in a pediatric hospital in México city. *Am. J. Med. Genet. 20*: 665-672.

Castilla, E.O., Mutchinik, O., Paz, J., Muñoz, E. and **Gelman, Z.** (1974). *Bol. of Sanit. Panam. 78* (6): 494.

Hall, J.G., Powers, E.K., McIlvaine, R.T. and **Ean, V.H.** (1978). The frequency and financial burden of genetics disease in a pediatric hospital. *Am. J. Med. Genet. 1*: 417-436.

Jiménez-Balderas, E., Salamanca-Gomez, F., Martinez-Apac, S. and **Bracho-Solis, M.** (1985). Estudio de malformaciones congénitas en 105,825 nacimientos consecutivos. *Bol. Med. Hosp. Infant. Mex. 42*: 744-747.

Mutchinick, O., Lisker, R. and **Baninski, V.** (1988). Programa mexicana de "Registro y vigilancia epidemiológica de malformaciones congénitas externas". *Salud Pública de México 30*: 88-100.

Organizacion Panamericana de La Salud (OPS). (1984). Prevención y control de las enfermedades genéticas y los defectos congénitos. Washington, D.C. Publicación científica No. 460.

Penchaszadeh, V.B. (1979). Frequency and characteristics of birth defects admissions to a pediatric hospital in Venezuela. *Am. J. Med. Genet. 3*: 359-369.

(Received March 16, 1994)