

The frequency of genetic diseases in a high risk ward in a pediatric hospital

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ABSTRACT

From March 1990 to January 1991, all patients admitted to a high risk ward in a pediatric hospital in Porto Alegre, RS, Brazil, were examined. The study had the following objectives: evaluate the frequency of admissions due to genetic diseases and determine the peculiarities of the admissions. All patients were submitted to a physical examination and their parents were interviewed, in order to obtain information about the family and reproductive histories. Among a total of 849 patients admitted, 12.5% had genetic, or partly genetic diseases, 68.7% had diseases caused by environmental factors, 5.9% had developmental anomalies, 8.4% were children with physiological disorders and 4.6% had no established etiological diagnosis.

Statistical analysis, comparing data from the genetic group and those from the control group, showed that the genetic patients were admitted earlier, stayed longer, were readmitted and died more frequently than the patients admitted due to other causes, representing a greater social and financial burden.

INTRODUCTION

Genetic diseases and congenital malformations are common admission causes in pediatric hospitals, especially in developed countries, where improvement of social and economic conditions has led to a decreased number of admissions due to infectious diseases.

During the last decades, several studies have been done to determine the frequency of genetic diseases in hospitals of developed countries, as well as in those of underdeveloped nations. Eleven to 54% of the admissions in hospitals of developed countries are due to genetic diseases (Scriver *et al.*, 1973; Day and Holmes, 1973; Reich *et al.*, 1974; Hall *et al.*, 1978; Fitzpatrick *et al.*, 1991). Lower frequencies are found in

studies of underdeveloped nations. In these countries infectious diseases and nutritional disorders are the main reasons for admissions (Barreiro *et al.*, 1976; Penchaszadeh, 1979; Carnevale *et al.*, 1985).

The small number of prospective studies published, as well as the lack of knowledge about frequency of admissions due to genetic diseases in high risk wards of pediatric hospitals in our country, motivated the present study.

MATERIAL AND METHODS

From March 1990 to January 1991, all patients admitted to a high risk ward (28 beds) in the Hospital da Criança Santo Antônio, Porto Alegre, RS, Brazil, were examined. The majority of these patients were less than three months old.

There were 849 first admissions and 92 readmissions. The patients were classified into five groups: 1) patients with genetic or partly genetic diseases; 2) patients with environmentally provoked disorders (infectious diseases, burns, trauma, etc.); 3) patients with developmental anomalies; 4) patients with physiological and transitory problems and 5) patients without a final diagnosis when discharged. Identification data, family and reproductive histories and information concerning the admission of each patient were obtained. Data was evaluated by means of chi-square, Fisher exact test, Student *t*-test, Mann-Whitney test and variance analysis (Kruskal-Wallis analysis), according to the variable studied (Zar, 1984). A probability of 0.05 or less was accepted as significant.

RESULTS AND DISCUSSION

Among the 849 patients admitted, 106 had genetic or partly genetic diseases; 583 had diseases caused by environmental factors; 50 had developmental anomalies (conditions thought to be malformations caused by abnormality in embryonic development of unknown etiology and for which, to our knowledge, recurrence risk had not been established, or for which the multifactorial nature of the condition was not conclusive (e.g. hernias, imperforate anus or renal anomalies, as defined by Hall *et al.*, 1978); 71 were children with physiological problems (gastroesophageal reflux and physiological jaundice) and 39 patients had no etiological diagnosis established when discharged.

As it was not possible to interview all the patients' parents and to examine all the patients, each variable studied has a different total number of cases.

Identification data

Thirty-eight percent of the patients in the genetic group came from outside Porto Alegre and the Porto Alegre region (cities located up to 50 km from Porto Alegre), while in the control group (patients with environmentally provoked disorders) only 11.9% came from these regions of Rio Grande do Sul State. The difference was significant ($\chi^2 = 48.74$; $P < 0.00001$). This shows that the Hospital da Criança Santo Antônio is a reference center for genetic patients in Rio Grande do Sul State, and that the families with genetic disorders have to travel greater distances to get appropriate care for their children. The same was observed by other

authors (Hall *et al.*, 1978; Carnevale *et al.*, 1985; Paskulin, 1989).

We observed that more males than females were admitted in both groups. Also, more whites were seen in both groups. No significant difference was found between the two groups for these factors (Table I). Hall *et al.* (1978), also did not find racial differences between patients with genetic diseases and those admitted to the hospital to treat non-genetic disorders. Deviation in sexual proportion has been found by several authors (Scriver *et al.*, 1973; Hall *et al.*, 1978; Penchaszadeh, 1979; Carnevale *et al.*, 1985; Paskulin, 1989). Carnevale *et al.* (1985) suggested that parents give preference to male children within the family when they seek medical care.

Table I - Patients' sex and race in a high risk ward in a pediatric hospital.

	Genetic disease group	Control group
Male	65	336
Female	41	247
White	90	469
Non-white	14	106

Genetic patients were admitted at an earlier age than the control group (Table II). As the present study was performed in a ward of patients with zero to three months of age, we could not compare data with the other authors which studied patients between zero and 12 or 18 years. Probably genetic patients were admitted earlier because of the severity of these diseases.

Table II - Patients' age (in days) in a high risk ward in a pediatric hospital.

Genetic disease group			Control group			Mann-Whitney test
N	Median	Range	N	Median	Range	
106	17.5	(1-98)	583	41	(1-193)	Z = -7.512; P < 0.00001

Family and reproductive histories

Paternal and maternal ages were not significantly different between the two groups. When paternal and maternal ages were classified according to the genetic diagnosis, no significant differences were

found, though the maternal and paternal ages were greatest in the group with chromosomal anomalies (Table III and IV). Only one patient with an X-linked recessive disease was found, and there were no patients with X-linked dominant disease. Because of this, these categories were excluded in Tables III and IV. Hall *et al.* (1978) also observed that the parents of patients with chromosomal anomalies were older, but the difference was not significant. Nevertheless, Carnevale *et al.* (1985) and Paskulin (1989) observed that the mean ages of parents of patients with chromosomal disorders were significantly greater than with other diagnoses.

Table III - Maternal age (in years), according to genetic diagnosis.

Diagnosis	N	Median	Range	Kruskal-Wallis test
Autosomal recessive	14	24	(15-38)	$\chi^2 = 6.07$; NS*
Autosomal dominant	31	26	(14-39)	
Chromosomal	9	38	(19-42)	
Multifactorial	40	24	(15-39)	

*NS = Not significant.

Table IV - Paternal age (in years), according to genetic diagnosis.

Diagnosis	N	Median	Range	Kruskal-Wallis test
Autosomal recessive	11	28	(15-41)	$\chi^2 = 6.81$; NS*
Autosomal dominant	31	26	(18-54)	
Chromosomal	8	41	(24-43)	
Multifactorial	39	29	(17-60)	

*NS = Not significant.

The consanguinity rate was greater (7.87%) in the group of genetic patients than in the control group (1.8%) (Fisher test, $P = 0.0051$). The rate found in the genetic group was similar to that observed by Paskulin (1989) and three times the one estimated for the Rio Grande do Sul's population (2.42%) by Salzano and Freire-Maia (1967). No differences were found between the two groups related to the types of consanguineous marriages, most of these marriages being between first cousins. The mean inbreeding coefficients in the genetic group and in the control group were, respectively, 0.0033 and 0.00084.

No differences were found between the reproductive histories of the genetic and control patients; also found by Paskulin (1989).

Admission data

Those patients with disorders of unknown cause received symptomatic treatments and were dispensed from further ambulatorial investigation and diagnosis. Most of the patients with genetic or partly genetic diseases had autosomal dominant or multifactorial conditions (Table V). The frequency of genetic or partly genetic diseases found in our study (12.5%) is similar to that observed by Reich *et al.* (1974) and Carnevale *et al.* (1985). Clearly genetic diseases (monogenic and chromosomal disorders) accounted for 1.99 to 7.3% of admissions in the reviewed literature (Day and Holmes, 1973; Scriver *et al.*, 1973; Reich *et al.*, 1974; Barreiro *et al.*, 1976; Hall *et al.*, 1978; Penchaszadeh, 1979; Carnevale *et al.*, 1985; Fitzpatrick *et al.*, 1991). The frequency of clearly genetic diseases that we found is similar to that seen by Scriver *et al.* (1973).

Table V - Frequency of admission, by cause of disease (N = 849).

Category	%
Autosomal recessive	1.7
Autosomal dominant	4.1
X-linked recessive	0.1
Chromosomal	1.2
Multifactorial	5.4
Developmental anomalies	5.9
Physiological conditions	8.4
Environmental origin	68.7
Unknown etiology	4.6

According to the literature, multifactorial disorders are responsible for 3.3% to 48% of hospital admissions (Day and Holmes, 1973; Scriver *et al.*, 1973; Reich *et al.*, 1974; Barreiro *et al.*, 1976; Hall *et al.*, 1978; Penchaszadeh, 1979; Carnevale *et al.*, 1985; Fitzpatrick *et al.*, 1991).

Genetic patients had longer periods of hospitalization (Table VI). The length of hospitalization varied significantly, depending on genetic diagnosis (Table VII). Using the minimal significant difference (Daniel, 1978; Campos, 1983) we determined that patients with autosomal recessive diseases and multifactorial conditions stayed longer than patients

Table VI - Length of hospitalization (in days).

Genetic disease group			Control group			Mann-Whitney test
N	Median	Range	N	Median	Range	
106	10.5	(2-146)	583	8	(1-115)	Z = -4.45; P < 0.00001

Table VII - Length of hospitalization, according to genetic diagnosis (in days).

Diagnosis	N	Median	Range	Kruskal-Wallis test
Autosomal recessive	14	31	(7-146)	$\chi^2 = 33.34$; P < 0.00001
Autosomal dominant	35	5	(2-33)	
Chromosomal	10	10.5	(4-33)	
Multifactorial	46	14.5	(2-57)	

with autosomal dominant diseases ($P < 0.05$). This could be explained by the severity of the autosomal recessive disorders and the surgical nature of most of the multifactorial disorders in our sample, leading to prolonged hospitalizations for these patients. Genetic patients are known to stay longer than other types of patients (Scriver *et al.*, 1973; Hall *et al.*, 1978; Penchaszadeh, 1979; Carnevale *et al.*, 1985; Paskulin, 1989; Fitzpatrick *et al.*, 1991).

The total number of admissions for genetic or partly genetic diseases was 129 (106 first admissions and 23 readmissions), while the total number of admissions for environmentally related diseases was 637 (583 first admissions and 54 readmissions). Comparing readmissions of patients between the two groups we observed that genetic patients were more often readmitted ($\chi^2 = 10.38$; $P < 0.01$). Similar results were observed by several authors (Scriver *et al.*, 1973; Hall *et al.*, 1978; Carnevale *et al.*, 1985; Fitzpatrick *et al.*, 1991). As the genetic patients stayed hospitalized longer and were more frequently readmitted, we concluded that their hospitalization costs were higher. Hall *et al.* (1978), Carnevale *et al.* (1985) and Paskulin (1989) also observed that the cost of hospitalization of genetic patients was higher.

A greater number of deaths was observed in the genetic patients' group (Table VIII). Several authors found a higher mortality for genetic patients when compared to patients admitted due to non-genetic diseases (Hall *et al.*, 1978; Carnevale *et al.*, 1985; Paskulin, 1989; Fitzpatrick *et al.*, 1991).

Table VIII - Frequency of deaths.

Deaths	Genetic disease group	Control group	Fisher test
Yes	7	1	P = 0.000012
No	99	582	

In conclusion, the results of our study showed that patients with genetic or partly genetic diseases were admitted earlier, came more frequently from outside Porto Alegre, had longer mean stays and more admissions, with a higher mortality rate. This suggests that genetic disease, although less frequent than disease caused by environmental conditions, leads to a considerable financial burden for the family and for society. As with infectious diseases, preventive measures (genetic counseling and prenatal diagnosis) could be the best solution for these problems.

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RESUMO

Durante o período de março de 1990 a janeiro de 1991, foram avaliados todos os pacientes admitidos em uma unidade de lactentes de alto risco do Hospital da Criança Santo Antônio, Porto Alegre, RS, Brasil, com o objetivo de determinar a frequência de admissões hospitalares devido a doenças genéticas, bem como avaliar as peculiaridades das internações destes pacientes. Todas as crianças foram examinadas, do ponto de vista clínico. Além disto, entrevistas foram realizadas com os familiares, a fim de se obter dados de história familiar e reprodutiva de todos os pacientes. Durante o período de estudo, foram admitidos 849 pacientes, sendo 106 (12,5%) devido a doenças genéticas; 583 (68,7%) com doenças provocadas por fatores ambientais; 50 (5,9%) com anomalias do desenvolvimento; 71 (8,4%) com condições fisiológicas e transitórias e 39 (4,6%) ficaram sem diagnóstico etiológico estabelecido.

As análises estatísticas, comparando as informações obtidas no grupo de pacientes com doenças genéticas e aquelas obtidas no grupo de pacientes com doenças ambientais (grupo controle), demonstraram que os pacientes com doenças genéticas são admitidos mais precocemente, permanecem mais tempo internados, reinternam mais vezes e apresentam uma mortalidade maior do que os pacientes com doenças ambientais, representando, portanto, um custo hospitalar e social maior.

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