

STUDIES ON POLYMORPHISM SEGREGATION IN NORTHEASTERN BRAZIL. II. PAIRS OF RELATIVES

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ABSTRACT

Two relatively large Northeastern Brazilian samples were analysed in order to study the intrafamilial behavior of several polymorphisms, through pairs of relatives and sex distributions. Except for samples which include more than one paired observation per family, no excess of significant departure from theoretical expectation was found. The excess verified both in mother x offspring and in sib pairs, when the entire offspring were included in the sample, testify to the sensitivity of the method to detect violations of the independence criterion. No associations with sex were detected for any of the polymorphic systems studied in both samples.

INTRODUCTION

During the last decade some unusual observations have been made on a few human polymorphic systems, such as a low frequency of identical Rh and ABO phenotypes in pairs of sibs (Valenzuela *et al.*, 1980; Valenzuela, 1981, Valenzuela *et al.*, 1980, Valenzuela *et al.*, 1982, Valenzuela and Harb, 1982, Valenzuela and Walton, 1985; Cifuentes and Valenzuela, 1986) as well as a significant sex - haptoglobin phenotype association (Amorim *et al.*, 1988). Some of these observations have been contested on several grounds (Cabello *et al.*, 1988, Morro-Furlani *et al.*, 1990).

The present paper aims to test for the presence of some of the reported population characteristics in two samples of Brazilian migrants and to ascertain the properties of the pairs of relatives approach employed in the above cited reports.

MATERIAL AND METHODS

Two samples of Northeastern Brazil Migrants, collected ten years apart were used in the analyses. The first one, (Hosp I), consisted of 1068 nuclear families, on which data on 15 polymorphisms (Diego, Duffy, Gm, Haptoglobins, Hemoglobin, Km, Kell, Lewis, Lutheran, MNSs, P, PTC, Rh, Secretor and Transferrin) were available (cf. Morton *et al.*, 1965; Krieger *et al.*, 1965; Yasuda, 1965). The second set (Hosp II), consisted of 1806 families with three genetic systems (Hp, MN and Secretor) (cf. Russo, 1972, Cabello, 1972).

All the subsequent analyses employed ITO conditional probability matrices (Li and Sacks, 1954) to provide expected values for the observed pairs of relatives. Six different pairs of relatives were used: a) total sib-pairs - all possible pairs within a sibship were formed, when the age difference between sibs was equal to or less than four years; b) only the first and the second child (also with an age difference of four or less years); c) one pair from each sibship, with an age difference of three or more years; d) the sibship was divided by the sex of the sibs, to test sex-polymorphism association; e) mother-child pair (in this case each of all possible pairs was taken as an observation); f) mother and one child chosen at random. All the values having an expected value of less than five were

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pooled in order to avoid inflation of type I errors. Gene frequencies were estimated by maximum likelihood from the pair matrices. The computer program utilized (ITO and SIB) are available from the "GENIOC" library, at the Department of Genetics, Instituto Oswaldo Cruz.

RESULTS AND DISCUSSION

No effect of sex on phenotype frequencies was detected in any of the polymorphic systems analysed in both samples (Tables I and II).

Table I - Chi-square values for comparisons between expected and observed values in pairs of relatives of the Hosp I population. Degrees of freedom are given in parentheses.

Genetic system	All sib-pairs	One pair of sib-ships	Pairs of sib-ships with > 3 years	Between sex	Mother all children	Mother one child
Diego	1.55 (2)	1.55 (2)	1.55 (2)	0.16 (1)	0.229 (2)	0.23 (2)
Duffy	30.42* (2)	2.66 (2)	5.21 (2)	0.33 (1)	19.78* (2)	0.86 (2)
Gamagl.	161.22* (76)	86.30 (76)	81.60 (76)	11.23 (8)	183.85* (61)	54.05 (61)
Haptogl.	20.80* (7)	7.07 (7)	5.78 (7)	4.00 (2)	9.55 (5)	4.17 (5)
Hemogl.	4.84 (7)	8.27 (7)	10.07 (7)	0.36 (2)	5.58 (5)	2.79 (5)
Inv (Km)	2.35 (2)	2.79 (2)	0.80 (2)	0.22 (1)	0.60 (2)	1.46 (2)
Kell	5.63 (7)	7.31 (7)	5.91 (7)	0.16 (2)	3.34 (5)	1.60 (5)
Lewis	4.67 (2)	2.59 (2)	2.39 (2)	0.24 (1)	3.56 (2)	0.43 (2)
Lutheran	1.36 (2)	1.82 (2)	5.19 (2)	0.06 (1)	1.66 (2)	0.24 (2)
MN	8.09 (2)	2.70 (7)	5.27 (7)	4.81 (2)	29.82* (5)	6.13 (5)
P	1.87 (2)	0.78 (2)	0.29 (2)	0.73 (1)	2.34 (2)	0.40 (2)
PTC	8.12* (2)	1.40 (2)	1.48 (2)	0.07 (1)	1.64 (2)	1.73 (2)
Rh-C	31.89* (7)	10.01 (7)	17.32* (7)	0.44 (2)	14.97* (5)	3.33 (5)
Rh-D	1.57 (2)	22.28 (2)	1.11 (2)	0.00 (1)	8.45* (2)	1.06 (2)
Rh-E	11.97 (7)	21.27* (7)	12.95 (7)	1.48 (2)	18.28* (5)	2.67 (5)
Ss ^{II}	3.00 (7)	6.78 (7)	4.79 (7)	3.67 (2)	23.70* (5)	2.33 (5)
Secretor	7.44* (2)	0.70 (2)	6.35* (2)	0.02 (1)	3.48 (2)	0.49 (2)
Transfer (7)	15.30* (7)	1.38 (7)	1.89 (2)	2.41 (5)	8.21 (5)	6.96 (5)

*Significant at the 5% level.

Table II - Chi-square values for comparisons between expected and observed values in pairs of relatives of the Hosp II population. Degrees of freedom are given in parentheses.

Genetic system	All sib-pairs	One pair of sib-ships	Pairs of sib-ships with > 3 years	Between sex	Mother all children	Mother one child
Haptogl.	20.82* (7)	4.34 (7)	5.12 (7)	1.27 (2)	20.29* (5)	4.16 (5)
MN	9.77 (7)	6.32 (7)	10.97 (7)	3.74 (2)	27.70* (5)	6.20 (5)
Secretor	1.21 (2)	1.50 (2)	2.09 (2)	3.62 (1)	3.22 (2)	0.70 (2)

*Significant at the 5% level.

There was a conspicuous concentration of significant departures from the theoretically expected values among tests which used multiple observations on the same nuclear families. Out of 42 tests, 17 were significant at the 5% level, while among the remaining analyses, which used only one observation per family, the number of significant deviations observed coincided with the figure expected by chance alone (three against an expected value of 3.15).

These facts indicate that non-independent observations introduce a significant bias, in such a way as to seriously inflate the observed proportion of type I errors. Although this fact can explain some of the results obtained by others, wrongly assigned paternity is also an important cause of significant departure from theoretical expectation derived from ITO matrices (Cabello *et al.*, 1988).

The above analyses show that former studies employing traditional segregation analysis (cf. Morton *et al.*, 1965) were less prone to biases and therefore these techniques should be preferred in studies of population dynamics, since, as shown above, samples of relative pairs are extremely sensitive to the violation of the independence criterium, inflating the number of "significant" departures from expected values, while segregation analysis takes into account the within family distribution of phenotypes, regardless of the family size or the heterogeneity of size among families.

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RESUMO

Duas amostras relativamente grandes do Nordeste Brasileiro foram analisadas visando a estudar o comportamento intra-familiar de vários polimorfismos, através de pares de parentes e testar possíveis

associações com o sexo. Excetuando as amostras que incluíam mais de um par de observações por família, nenhum excesso de diferenças significantes entre os observados e os esperados pela teoria, foi encontrado. Os excessos verificados nas análises de mãe e todos os filhos e pares de irmãos, quando a irmandade total foi subdividida em todos os possíveis pares, testemunham a favor da grande sensibilidade do método diante da violação do critério de independência de observações. Nenhuma associação sexual foi detectada em qualquer dos sistemas polimórficos estudados, em ambas as amostras.

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