ABO Blood Groups : Influence of Maternal Phenotype on the Consecutive Sibs

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KEY WORDS ABO System. Segregation. Sib-Sib Matrix.

ABSTRACT A sample of 312 consecutive sib pairs classified according to maternal phenotype was studied for segregation deviations of the ABO system. Approximately 60 per cent of the sibs shared the same phenotype. The sub-samples of pairs born to A, B and O mothers as well as the total sib-sib matrix were found to be in perfect harmony with the expected segregation. Both AO and BO mothers segregated preferentially in favour of *A* and *B* alleles.

INTRODUCTION

A number of theories have been put forward to explain the maintenance of polymorphic forms of the ABO blood group system but so far no satisfactory explanation has been obtained (Cavalli-Sforza and Bodmer, 1971). Foetal losses, both due to ABO-incompatibility (Grubb and Sjostedt, 1955; Schapp el al., 1984; Valenzuela and Walton, 1985) and haemolytic disease of the newborn (Sever, 1969; Race and Sanger, 1975) can affect heterozygote fitness. The haemolytic disease of the new born occurs mostly in AO and BO new borns of the O mothers which lack both A and B antigens but possess both anti-A and anti-B IgG antibodies, which play havoc by destroying the new born's erythrocytes. However since the role of selection during the early stages of foetal development is not consistently demonstrated nothing can be said with surity about its evolutionary trend. The present study is designed to explore the ABO distortions in the sib-sib matrices grouped according to the mother's phenotype in order to separate the maternal effects.

MATERIAL AND METHODS

Data on sib pairs (n=312) as well as maternal phenotype was collected from the families residing in the Punjabi University Campus, Patiala City and the Urban Estates of Patiala. Most of these families have only 2 and rarely 3 children and all the sibs in this study are consecutive sibs, except the ones, where due to unknown embryo losses, consecutive sibs do not correspond to consecutive pregnancies.

The ABO typing was done following the standard techniques of haemagglutination reaction. Sib pairs are named according to their phenotypes. Thus A-O is the pair, where the first sib is A and the consecutive one is O.

Statistical Analysis

ABO allele frequencies were calculated following the methods of Yasuda (1984) and the maximum likelihood estimates of Li (1976). Assuming Hardy Weinberg equilibrium, the total matrix was divided into three, according to the phenotype of the mother (A, B and O) excluding the AB matrix due to small size of the sample.

The chi-square test was applied on the sib pairs to check the significance of deviations from expected Hardy Weinberg proportions. The difference in ABO phenotypic frequencies between consecutive sibs was tested by a modified Z test for proportions allowing for sib-sib covariance (Valenzuela and Harb, 1982; Cifuentes et al., 1986).

RESULTS AND DISCUSSION

The ABO allele frequencies for the consecutive sibs are given in table 1. The average values of *A*, *B*, *O* for both sibs are 0.17775, 0.27738 and 0.54486, respectively. The frequ-

Table 1: Distribution of ABO blood groups in sib pairs (n=312)

n = 312	*Phenotypes*				*Allele frequencies*	$\chi^2_{(1)}$	*S.E.*	*Z value*
	A	*B*	*O*	*AB*				
Ist Sib								
Obs.	72	127	78	35	*A* 0.19017	0.0960 (p>.80)	0.01655	1.047 (p<0.05)
Exp.	70.78	126.68	78.83	36.52	*B* 0.30785		0.02037	2.108 (p >0.05)
					O 0.50198		0.02250	2.635 (p> 0.01)
IInd Sib								
Obs.	69	110	107	25	*A* 0.16593	0.0032 (p> 0.90)	0.01569	
Exp.	69.19	110.24	106.77	25.79	*B* 0.24878		0.01865	
					O 0.58529		0.02149	
Average values for both sibs :					*A* = 0.17775	*B* = 0.27738	*O* =0.54486	

ency of 'B' appears to be slightly on the higher side in the first sib and that of 'O' in the second one but not significantly so (χ^2 = 5.82916, df=3, 0.20> p> 0.10, Table 2), when we apply the simple chi-square test however the values of the Z test for the difference in A, B and O groups between the sibs are : 1.047 (p<.05), 2.108 (p>.05) and 2.635 (p>0.01), which are significant for both B and O group (The value of Z at 0.05 level is 1.96). The Z test was applied since simple chi-square test does not give covariance between the two samples and hence results in increasing the type II statistical error.

Pairs in which sibs shared ABO phenotype were 188 (60.25%) and 124 (39.75%) pairs did not share it. The observed sib-sib matrix was found to be in Hardy Weinberg equilibrium (Table 3). Table 4 shows the sib-sib matrix

Table 2: Comparison of ABO blood types in sib pairs

N=312	*Phenotypes*				*Total*
	A	*B*	*O*	*AB*	
Ist Sib					
Obs	72	127	78	35	312
Exp.	70.5	118.5	92.5	30.5	
IInd Sib					
Obs.	69	110	107	26	312
Exp.	70.5	118.5	92.5	30.5	
Total	141	237	185	61	624

$\chi^2_{(3)}$ = 5.82916 (p>0.20)

from A mothers. Preference for paternal *B* allele was observed in some cases but no significant deviations from the expected were seen in any of the sib-pairs in our data on Punjabi population for both A and B mothers (Table 5). Whereas Kirk (1955), Valenzuela and Walton (1985) and Cifuentes and

Table 3: ABO blood group : Sib-sib matrix

IInd Sib	*AB*			*A*			*B*			*O*			*Total*
Ist Sib	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	
AB	12	9.20	0.8522 (p>.90)	8	9.71	0.3011 (p>.975)	12	13.54	0.1752 (p>.99)	3	2.55	0.0794 (p>.955)	35
A	6	6.62	0.0581 (p>.999)	41	40.66	0.0028 (p<.9995)	9	8.48	0.0319 (p>0.999)	16	16.25	0.0035 (p<.9995)	72
B	7	8.04	0.1345 (p>.99)	11	10.06	0.0878 (p>.995)	78	77.40	0.0047 (p<.9995)	31	31.50	0.0080 (p<.9995)	127
O	1	0.82	0.0395 (p.999)	9	0.13	0.0019 (p.9995)	11	11.16	0.0023 (p<.9995)	57	56.89	0.0021 (p<.9995)	78
Total		26			69			110			107		

$\chi^2_{(13)}$ = 1.789 (p<.9995)

Table 4: ABO blood group : Sib-sib matrix in A mothers

IInd Sib	*A-Mothers*												
	AB			*A*			*B*			*O*			*Total*
Ist Sib	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	
AB	3	2.95	0.0008 (p<.9995)	3	3.03	0.0003 (p<.9995)	5	5.03	0.0002 (p<.9995)	1	0.98	0.0004 (p<.9995)	12
A	5	2.85	1.6219 (p<.70)	25	26.13	0.0489 (p>.999)	1	2.93	1.2713 (p>.80)	9	8.1	0.1000 (p>.995)	40
B	5	2.98	1.3693 (p>.80)	3	4.40	0.4455 (p>.95)	5	6.26	0.2536 (p>.975)	3	2.36	0.1736 (p>.99)	16
O		—		3	2.69	0.0357 (p>.999)	3	2.69	0.0357 (p>.999)	9	9.27	0.0079 (p<.9995)	15
Total		13			34			14			22		

$\chi^2_{(13)} = 5.3651$ (p>0.975)

Valenzuela (1986) had observed an excess of B children in A mothers and *vice-versa*, an observation which they tried to explain on the basis of hypothetical system of maternal tolerance induced early in pregnancy to the paternal gene. Our results on O mothers are presented in table 6. No significant deviation from the expected were observed.

In normal course, the segregation of AO and BO mothers should be 1/2.A : 1/2.O and 1/2.B : 1/2.O, respectively. A mother with blood group A who delivered a B or O child must necessarily be heterozygous and her segregation in the second sib can thus be tested. The same is true for B mothers. In AO mothers, some O eggs are fertilized by A sperms from fathers, therefore these A newborns from A mothers must be subtracted from the number of A infants born to A mothers and added to O eggs. The number which must be subtracted can be calculated from the expected Hardy Weinberg proportion. Thus the proportion of A infants born to AO mothers who segregated the A eggs will be $A+O$ $(2A+O)$ or 0.802 and the ones who segregated O eggs will be A $(2A+O)$ or 0.198. Similarly the estimated proportions in BO mothers for B allele will

Table 5: ABO blood groups : Sib-sib matrix in B mothers

	B-Mothers												
IInd Sib	*AB*			*A*			*B*			*O*			*Total*
Ist Sib	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp*	χ^2	
AB	8	4.59	2.5333 (p>.50)	2	4.26	1.1990 (p.60)	6	7.85	0.4360 (p>.95)	2	1.30	0.3769 (p>.95)	18
A	1	0.41	0.8490 (p>.90)	2	2.07	0.0023 (p<.9995)	1	1.51	0.1723 (p>.99)	3	3.01	0.00005 (p<.9995)	7
B	4	1.98	2.0608 (p>.60)	1	2.97	1.3067 (p>.80)	41	42.23	0.0358 (p>.999)	24	22.82	0.0610 (p>.999)	70
O		—			—		10	10.46	0.0202 (p>.9995)	9	8.55	0.237 (p>.9995)	19
Total		13			5			58			38		

$\chi^2 = 9.077$ (p >0.80)

Table 6: ABO Blood Groups : Sib-sib matrix in O mothers

	O-Mothers									
IInd Sib	*A*			*B*			*O*			*Total*
Ist sib	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	*Obs.*	*Exp.*	χ^2	
A	9	8.57	0.0216 (p>.99)	2	1.42	0.2349 (p>.90)	7	7.37	0.0186) (p>.995)	18
B	1	0.57	0.3244 (p>.90)	15	14.73	0.0049 (p.999)	6	6.18	0.0052 (p>.999)	22
O	4	3.90	0.0026 (p>.999)	2	1.92	0.0033 (p>.999)	35	35.08	0.0002 (p>.9995)	41
Total		14			19			48		

χ^2 = 0.6157 (p>.0.999)

be $(B+O)$ $(2B+O)$ *i.e.* 0.747 and for O=.253 $(B/2B+O)$.

Table 7 shows that AO mothers showed a tendency to segregate preferentially *A* allele in both the sibs and significantly more in the second one (χ^2 = 4.082; df=1 p>0.05). Tendency was the same in BO mothers–segregating preferentially the *B* allele in the first =38.2273; df=1 p<0.0005) as well as in the second sib (χ^2 = 13.1364; df=1 p <0.0005, Table 8).

Our results in the case of segregation of allele in AO and BO mothers differ from those of Cifuentes and Valenzuela (1986) who observed preferential segregation for *O* allele. However, the values may be different simply due to difference in the incidence of ABO blood group alleles in Chilean and North Indian populations. Whereas the incidence of *B* is very high in North India (approximately 30 per cent) it occurs with a very low frequency in Chile (only around 5 per cent). Similarly *O* allele which is present in 77 per cent of the Chilean group is comparatively much less in Punjab (50 per cent). The preferential segregation for O in B mothers in Chilean data may be due to selective forces favouring the *O* allele in that population. The reverse may be true for Punjabi group, the selection favouring the *B* allele in our data.

Table 7: AO mothers segregation

	Segregation				
	A		*O*		$\chi^2_{(1)}$
	Obs.	*Exp.*	*Obs.*	*Exp.*	
Ist Sib	34	29	24	29	1.724[1]
IInd Sib	31	24	17	24	4.082[2]

1. (p>0.20) 2. (p>0.05)

Table 8 : BO mothers segregation

	Segregation				
	B		*O*		$\chi^2_{(1)}$
	Obs.	*Exp.*	*Obs.*	*Exp.*	
Ist Sib	73	44	15	44	38.2273[1]
IInd Sib	61	44	27	44	13.1364

1. Significant

Criticism of the present results may arise from a statistical point of view. Expected numbers under 5 may invalidate the chi-square analysis. However Lewontin and Felsenstein (1965) demonstrated that the inclusion of figures lower than 5 do not alter significantly the probabilities of chi-square distribution.

CONCLUSIONS

The main results can be summarized as follows :

i) The incidence of blood group B was found to be higher in the first sib whereas blood group O was found to be more common in the second sib.

ii) Both AO and BO mother segregated preferentially in favour of *A* and *B* alleles, respectively and significantly so

in the case of B mothers. The results can be explained on the basis of known incompatibility system.

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