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ABO blood groups, sex ratio and intrauterine development

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Genetica. — *ABO blood groups, sex ratio and intrauterine development.* Nota di FULVIA GLORIA-BOTTINI, ERMINIA CARAPELLA-DE LUCA, MARCELLO ORZALESI e EGIDIO BOTTINI, presentata (*) dal Socio G. MONTALENTI.

RIASSUNTO. — Lo studio di due serie indipendenti di neonati di razza Caucasica ha mostrato che le femmine di gruppo B compatibili con la loro madre hanno un peso inferiore rispetto alle altre classi di neonati di sesso femminile e che il loro numero è più basso rispetto all'atteso calcolato sulla base delle frequenze geniche nel sistema ABO.

I dati suggeriscono che durante la vita intrauterina, le femmine di gruppo B compatibili con la madre hanno un accrescimento più lento ed una ridotta probabilità di sopravvivenza rispetto alle altre classi di zigoti. Questo svantaggio relativo potrebbe spiegare l'elevato rapporto sessi osservato tra i neonati compatibili di gruppo B.

We have recently confirmed that the sex ratio in B group infants compatible with their mothers is higher than in other classes of infants [1]. The present analysis shows that the proportion of B-compatible females is lower than expected on the basis of ABO gene frequencies and that these infants have a lower birth weight as compared to other classes of newborn females.

MATERIAL AND METHODS

Two serie of Caucasian newborn infants previously studied [1] have been considered for the present analysis. The first series of 1113 subjects was obtained from the population of New Haven (Conn. U.S.A.) during the years 1968–1971. The series included three groups of infants: *a*) consecutive for all births; *b*) consecutive only for ABO-incompatible births; *c*) consecutive only for Rh-incompatible births. The second series of 676 infants was obtained. in Rome (Italy) during the years 1971–1972 and was consecutive for all births. The ABO and Rh phenotypes were determined for each infant at birth and for its mother.

Infants with a gestational age equal to or greater than 37 weeks, weighing 2.5 Kg or less, were clinically considered growth retarded (light-for-dates, LFD) [2].

Statistical analyses were carried out according to SPSS programs [3] on an IBM 370/158 computer.

(*) Nella seduta del 6 dicembre 1980.

Results

Table I reports a short summary of the sex ratio relations at birth previously described [1], ABO compatibility status and fetal ABO phenotype. A very high sex ratio in B-compatible infants is observed.

ABO gene frequencies were practically identical in the two series of Caucasian infants considered. Moreover, when these infants were divided with respect to sex and ABO blood groups, mean birth weight and mean gestational age did not appear significantly different in the two series. Therefore these were considered cumulatively for the present analyses.

Table I.

Sex ratio (SR) at birth. The relation with ABO compatibility status and fetal ABO phenotype. (1)

Caucasian Populations		SR	Newborns N°
ABO-compatible	B	2.103	90
	Others	1.052	1.067
ABO-incompatible	B	1.277	189
	Others	1.005	443
Other Populations			
ABO-compatible	B	1.400	36
	Others	0.951	361
ABO-incompatible	B	1.056	74
	Others	1.083	100

Table II shows the observed and expected proportions of B phenotype in ABO-compatible infants, separately for males and females. A decreased proportion of B-compatible females as compared to Hardy-Weinberg expectations, is observed ($p < 0.02$). The proportion of B-compatible males is higher than expected; the difference, however, is not statistically significant.

TABLE II.

Observed and expected proportion (%) of B group infants in ABO-compatible newborns. Observed proportions are reported for males and females separately. Observed numbers are shown in brackets. Expected proportions were calculated on the basis of ABO-gene frequencies.

	NEW HAVEN			ROME			ALL INFANTS
	Expected	Observed	Percent variation	Expected	Observed	Percent variation	Mean weight percent variation
Males	8.7	10.9 $\left\{\frac{35}{322}\right\}$	+ 25.3	7.8	9.1 $\left\{\frac{26}{286}\right\}$	+ 16.7	+ 21.3
Females		4.5 $\left\{\frac{13}{290}\right\}$	— 48.3		6.2 $\left\{\frac{16}{259}\right\}$	— 20.5	— 35.2

TABLE III.

Birth weight (grams), gestational age (weeks) and percentage of LFD in relation to sex, ABO phenotype and compatibility status. Pooled data from all Caucasian infants.

		BIRTH WEIGHT			GESTATIONAL AGE			PROPORTION OF LFD
		Mean	S. D.	N° of infants	Mean	S. D.	N° of infants	
B-compatible	males	3302	421	54	39.2	1.41	45	1.8
	females	2955	671	29	38.7	2.22	27	10.3
Other infants	males	3373	548	788	39.2	1.93	674	3.3
	females	3201	539	807	39.4	2.10	702	6.6

Table III shows the mean values and the standard deviations of birth weight and gestational age and the proportion of LFD for B-compatible and other classes of infants. Males and females are analyzed separately. B-compatible females show a significantly lower birth weight as compared to other classes of females ($p < 0.02$). Also the mean gestational age of these infants appears lower as compared to that of other infants; the difference, however, does not attain the level of statistical significance. Among males no significant difference of mean values is observed between B-compatible and other classes of infants. B-compatible female infants show a proportion of LFD greater than that of all other classes of infants. The difference, however, is not statistically significant.

DISCUSSION

Previous investigations on the relation between birth weight and ABO blood groups have given inconsistent results. Plotkin [4] studied a series of 1033 full-term (FT) and 100 low-birth-weight (LBW) infants and observed a higher incidence of B phenotype among LBW. The proportion of females among LBW was higher than among FT babies. Data on feto-maternal compatibility status were not reported. Kothari *et al.* [5] examined 200 consecutive live-born-infants and found that AB infants tended to have the lowest birth weight. More recently Uzel and Neyzi [6] studied 506 randomly selected newborn infants and did not find any effect of blood group on birth weight. In these studies the possible effect of feto-maternal compatibility status on the relation between ABO phenotype and birth weight was not considered.

We think that in any investigation concerning the role of blood groups in intrauterine life, the feto-maternal compatibility status should be always considered. Moreover, since strong selective phenomena are not expected, large samples should be examined in order to detect significant distortions.

The present data, obtained on relatively large samples from two different populations, indicate that a relation between ABO blood groups and intrauterine development may in fact exist and that this relation may be influenced by the sex of the infant and by the feto-maternal ABO compatibility status. The observations suggest that during intrauterine development B-compatible females may experience some disadvantage resulting in a relatively slow growth rate and in reduction of survival rate. The high secondary sex ratio observed in B-compatible infants may be a consequence of these factors.

Previous studies suggest that fetuses unlike their mothers may have an increased chance of survival and that genetical dissimilarity with the mother may favour the implantation of the blastocyst [7, 8]. It has also been suggested that the ABO-compatible male blastocyst could implant more successfully than females owing to differences with their mothers in Y-linked antigens [8]. On the basis of the pattern of interaction between human placental alkaline phosphatase (Pl) and ABO system polymorphisms [9, 10, 11], we

have put forward the hypothesis that fetuses carrying the B factor may show a better immunological isolation [12]. This could represent an advantage in the presence of maternal-fetal blood group incompatibility. On the contrary, B group individuals compatible with their mothers, especially the females, may experience a relative disadvantage at implantation and/or during intrauterine development. The above data seem to give some support to our hypothesis.

The problem of immunoregulation of pregnancy is still largely unsolved [13]. We think that further studies in the area of the maternal-fetal relationship should take into account ABO, Pl, sex and possibly also other polymorphic systems and their interactions. Such studies could be of interest in elucidating the forces which maintain these polymorphisms and their role in the maternal-fetal relationship.

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