ABO & RH BLOOD GROUPS & TOXAEMIAS OF PREGNANCY

by

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and

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Landsteiner's discovery of the Blood Groups in 1900 opened up new horizons in many fields of study, particularly in Genetics and Medicine.

That the possibility of an association between blood groups and diseases has not been overlooked is proved by the numerous reports of work done in this direction since 1920. The results obtained, though not very encouraging, have been quite interesting. It might be emphasised here that the negative findings have proved to be more than valuable. Though work on blood groups and diseases have been subject to a spate of criticism by Manuila, it has not deterred further work, and now present trends involve associations not only with the ABO and Rh blood groups but all the other nine blood group systems as well. There can be no doubt that Immunologists, Clinicians and Geneticists alike will benefit as a result of all this work. The study of blood groups and diseases has been done and encouraged predominantly by British workers. Workers in other countries include Koster, Sinderup and Seele of Denmark, Hollander of Switzerland and Buckwalter et. al. of the U.S.A. The result of all this work has been conflicting and lacks consistency. Aird, Bentall et. al. were the first to report a definite association between gastric cancer and group A and between duodenal ulcer and group O. Association between blood groups and various other diseases such as pernicious anaemia, diabetes mellitus, rheumatic fever, etc. have been studied, but whether associations really exist still remains a moot point.

In this study, we have tried to find out whether any association between the ABO and Rh blood groups and toxaemias of pregnancy exists. Pike and Dickins in 1954, had already done such a survey in England. At first, they reported a marked preponderence of group O in toxaemic patients. Later on in 1955, and finally in 1956, on re-evaluating their work, they concluded that there was no significant difference in the ABO and Rh blood group frequencies in toxaemic and non-toxaemic patients.

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Choice of Controls

In all studies on association between blood groups and disease the use of proper controls is very essential. According to general opinion, the control series should be taken from the same strata of the population as the patients and should have the same anthropological and ethnological background. Why this should be so is still a subject of controversy. The three types of controls generally used are: (1) patients from the same hospital with diseases other than the one under survey, (2) blood donors from a transfusion service, (3) sibs of the propisitus. It is obvious that none of these controls is perfect, for in no series is it possible to maintain an equilibrium of conditions between the disease series and the controls. This is well illustrated in our study. While the hospital series proves to be ideal with respect to the pregnancy factor (the study was carried out on pregnant women), this object is not achieved with the blood donor series, as most of them were men. Both controls seem to be adequate with respect to population, stratification, etc. In our survey we have used two types of controls, (1) pregnant women and (2) blood donors from the Voluntary Blood Donor Service of Haffkine Institute. Consistency of results using different control series is quite essential. The danger of using different controls is shown by the study of the ABO blood groups and duodenal ulcer. When blood donors were used as controls, an association was found between group O and duodenal ulcer patients, but when sib-ship studies were used, no association was found. It may be mentioned here that statistical methods, though invaluable, often fall wide of the mark, but this is inevitable.

Material and Method

The survey was carried out at the N. W. Maternity Hospital, Bombay, from August 1961 to August 1962. An average of 40 women are registered daily. The ABO and Rh blood groups of these women are done as a routine procedure. The distribution of the ABO and Rh blood groups in 14,004 of these admissions was evaluated. During this period 562 patients developed toxaemia of pregnancy (178 primiparas and 384 multiparas). The toxaemias of pregnancy are characterized by several features, such as high blood pressure, oedema, albuminuria, changes in the visual field, and liver, kidney and brain damage in the more severe cases. In our series a patient was considered toxaemic if she possessed any two of the following:

(i) A blood pressure of 140/90 mm. of Hg or more during the 3rd trimester.
(ii) Clinical oedema or a weight gain of more than 1 lb. per week in the 3rd trimester.
(iii) Albuminuria — in a catheter specimen. Cases of eclampsia, and immunisation were excluded.

The following was recorded for each patient:

(1) Name.
(2) Age.
(3) Parity.
(4) Type of delivery.

(5) Caste.
(6) ABO and Rh blood groups.

The caste was noted in order to ensure similar distribution in the control series.

The method employed for ABO blood grouping was the tube technique using potent anti-A and anti-B sera. The enzyme technique was followed for Rh grouping (papain — being the enzyme used). Blood grouping techniques are now well standardized, so that any error due to blood grouping would be almost negligible.

Results

The procedure employed in analysing the data was to compare the blood type frequencies of the patients with those of the control series. The statistical significance of the difference between the patient and control blood type frequencies was then calculated by the chi-square method. In our series no statistically significant difference emerged. A variation in the distribution of the ABO blood groups is noted in the two control series, particularly with respect to group O. In the hospital series, group O frequency is 32%, while in the donor series, it is 37%. There is a slight excess of group B over group A in the hospital series, while in the donor series the percentage is the same. The percentage of group AB is 8 in the hospital series and 7 in the donor series. Variations of the type found in these two series is to be expected since the blood donor series is comparatively small. Table I shows the distribution of the ABO and Rh blood groups in the disease series and the comparison with hospital controls.

TABLE I

Distribution of ABO and Rh Blood Groups in Toxaemic and Non-toxaemic Patients

(Control taken from Hospital Patients)

Group	Non-toxaemic		Toxaemic		% increase of tox. over non-toxaemias
	No.	%	No.	%	
O	4481	32.00	199	35.41	10.66
A	4015	28.67	152	27.05	— 5.65
B	4267	30.47	162	28.82	— 5.42
AB	1241	8.86	49	8.72	— 1.58
Total	14004	100.00	562	100.00	
Rh+	13111	95.22	540	96.09	.91
Rh—	658	4.78	22	3.91	—18.20
Total	13769	100.00	562	100.00	

There is an increase of group O in toxaemic patients, and a slight decrease of A and B patients. The percentage of group AB is the same in toxaemic and non-toxaemic patients. Table II compares the toxaemic series with the blood donor series. Here, the percentage of group

TABLE II

Distribution of ABO and Rh Blood Groups in Toxaemic and Non-toxaemic Patients

(Control taken from Haffkine Institute Voluntary Blood Donor Service)

Group	Non-toxaemic		Toxaemic		% increase of tox. over non-toxaemias
	No.	%	No.	%	
O	367	37.37	199	35.41	— 5.24
A	270	27.50	152	27.05	— 1.64
B	268	27.29	162	28.82	5.61
AB	77	7.84	49	8.72	11.22
Total	982	100.00	562	100.00	
Rh+	934	95.11	540	96.09	1.03
Rh—	48	4.89	22	3.91	—20.04
Total	982	100.00	562	100.00	

O is lower in the disease series. There is a slight increase in group B and AB of the disease series. On the whole, no statistically significant difference has been found using either series as controls. With hospital patients as controls X2 for 3 degrees of freedom for the ABO blood groups = 2.9492, probability = $.30 < P < .50$, and for the Rh blood group for 1 degree of freedom X2 = .08923, probability = $.30 < P < .50$. Using Haffkine series X2 for the ABO blood groups with 3 degrees of freedom = 1.0419, $P = .70 < P < .50$, and for the Rh blood groups with one degree of freedom X2 = .7825, $P = .30 < P < .50$. A comparison of group frequencies on the basis of parity also failed to show any statistically significant difference. X2 for the ABO blood groups = 1.8280, and for the Rh blood group = .0170, $P = .80 < P < .90$.

TABLE III

Distribution of ABO and Rh Blood Groups in Toxaemic Patients with respect to Parity

Group	Primiparas		Multiparas		% increase of primi. over multiparas
	No.	%	No.	%	
O	56	31.46	143	37.24	—15.52
A	52	29.21	100	26.04	12.17
B	54	30.34	108	28.13	7.86
AB	16	8.99	33	8.59	4.66
Total	178	100.00	384	100.00	
Rh+	171	96.07	368	95.83	0.25
Rh—	7	3.93	16	4.17	— 5.76
Total	178	100.00	384	100.00	

TABLE IV

Statistical Analysis in Terms of Chi-square and P

Type of series	Bl. Gr.	Degrees of freedom	Chi-square	P
Tox. series (control from Hospital patients)	ABO	3	2. 9492	$.30 < P < .50$
	Rh	1	0. 8923	$.30 < P < .50$
Tox. series (control from Haffkine blood donors)	ABO	3	1. 0419	$.70 < P < .80$
	Rh	1	0. 7825	$.30 < P < .50$
Primipara and multipara series	ABO	3	1. 8280	$.50 < P < .70$
	Rh	1	0. 0170	$.80 < P < .90$

Discussion

It is important to know whether an association between blood groups and toxaemia of pregnancy is causal or co-incidental. One might presume the toxaemia of pregnancy to be due to an antigen-antibody reaction between foetus and mother, or that the antibodies themselves behave as active chemical agents. Such possibilities may be readily dismissed, as evidence to the opposite is overwhelming. It would be interesting to know whether toxaemia is due to the mother bearing a heterospecific foetus, the placenta acting as a means of exchange between foetus and mother. It is known now that the placenta allows the passage of albumin or incomplete antibodies alone, as these have a lower molecular weight, being of the 7 S gamma globulin fraction. The antibodies of the ABO system usually exist as the saline type. They do not cross the placenta as they are of the 19 S type. A difference in secretor status between foetus and mother might also be one of the causes of toxaemia. In this respect more light would have been thrown on the subject if a study of the secretor status of mother and child were done. But since our study included only the ABO and Rh blood groups, no such survey was carried out. Toxaemia is often a cause for foetal loss, so also is immunisation. Immunisation together with toxaemia increases this danger, but is seems fairly obvious that immunisation, rather than toxaemia, is the primary cause for foetal loss. If toxaemia of pregnancy is due to an abnormal water and electrolyte balance, as Dieckmann believes, then the ABO and Rh blood groups would seem to have no direct relationship.

A more sensible approach to the problem would be to regard the blood groups in relation to natural selection. The blood groups are examples of balanced polymorphism, and association between blood groups and diseases could exist. The opinion held by most Geneticists is that, since most of the diseases found to be associated with blood groups, act during adult life, selection can have little effect. The principal mechanisms of selection, which maintains the ABO poly-

morphisms, act during foetal or early post-natal life, and associations between blood groups and adult diseases are at most secondary selective effects.

Summary

The ABO and Rh blood group distribution in 562 toxaemic patients was studied. No statistically significant difference in the ABO and Rh blood group distribution in toxaemic and non-toxaemic subjects was observed, using two types of controls, (1) pregnant women and (2) blood donors.

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References

1. Aird, I., Bentall, H. H., Mehigan, J. A. and Roberts, J. A. Fraser: Br. Med. J. 2: 315, 1954.
2. Balme, R. H. and Jennings, D.: Lancet, 1: 1219, 1957.
3. Buckwalter, J. A., Naifeh, G. S. and Acrer, J. E.: Br. Med. J. 2: 1023, 1962.
4. Cohen, B. H. and Thomas, C. B.: Bull: Johns Hop. Hosp. 110: 1, 1962.
5. Dieckmann, W. J.: Toxaemias of Pregnancy, St. Louis, 1942, C. V. Mosby Co. 19 and 330.
6. Manuila, A.: J. Am. Med. Ass. 167: 2047, 1958.
7. Pike, L. A., and Dickins, A. M.: Br. Med. J. 2: 321, 1954.
8. Race, R. R. and Sanger, R.: Blood Groups in Man. Oxford, 1962, Blackwell Scientific Publications p. 397-9.