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A STUDY OF THE ROLE OF ABO INCOMPATIBILITY IN THE
CAUSATION OF ABORTION

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Introduction

Abortion is a very important and common clinical problem. Nesbitt (1968) observed that about 15% of foetuses are lost before they reach the period of viability and it is natural that its cause must be properly pinpointed.

Review of Literature

Darrew (1938) was the pioneer to establish the role of immunological factors in causing haemolytic disease of the new born. According to him this is a result of maternally formed antibodies against some component of foetal red blood cells. Prior to this, alteration of anti A and anti B antibody titre in the sera of puerperal women was noted by Dienest (1905), Jonsson (1936), Smith (1945) and Orzsco (1948).

Some increase in the incidence of spontaneous abortions was noted by Levine (1945), Grubb and Sjoostedt (1955), Matsunage & Itoh (1958). They also said that blood groups incompatibility may be one of the factors causing unexplained sterility.

Hirzfeld (1945) observed that the couples with father of group A and mother of group O had a higher incidence of abortion and still-birth as compared to couples with O group father and A group mother.

Stratton & Reuten (1955) observed that anti A and anti B antibody titre increases with pregnancy if the foetus is group A or B, in group O mothers.

Wiener *et al* (1960) followed a number of families who had newborns with haemolytic disease due to ABO incompatibility. In these families the distribution of group A and group B was almost equal and incidence of group O was low in the fathers, whereas all the mothers

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except one, had blood group O and all the affected babies had either group A or group B.

Wren and Vos (1961) studied blood group incompatibilities as a cause of abortion in Australia. Out of 122 cases of abortion, 45% showed ABO incompatibility as compared to 30% of their control cases.

Material and Method

Two hundred cases of abortion were studied, showing no obvious cause for miscarriage. Only those cases of abortion were studied who did not have more than 3 live births before the first miscarriage. (The same criteria for selection of cases was undertaken by Wren and Vos 1961).

Proper general and systemic examinations of each patient was done. V.D.R.L. test of both husband and wife was carried out, fasting blood sugar and blood urea were done wherever necessary and all cases showing abnormal tests were excluded from the study.

ABO blood grouping and Rh typing of both husband and wife was done. In ABO incompatible couples anti A and anti B antibody titres were determined by making serial dilutions of mother's serum. Thrice washed fresh group A red cells were added to the serum of group B mothers, and group B cells to the serum of group A mothers. For group O mothers two rows of tubes were set up; to one group A and to the other group B cells were added. The control tube contained equal volumes of saline and red blood cells. The tubes were kept in water bath for half an hour at 37°C and were examined for agglutination microscopically. The titre of antibody was the maximum dilution where agglutination started.

Fifty-five couples who had one or more full term deliveries and no abortions

were also examined in the same way to serve as controls.

Observations

A total of 200 couples with history of spontaneous abortion were studied out of which 140 (70%) were such where the mating was incompatible (An incompatible mating means that the husband's red cells contain some blood group factor which is not found in the red blood cells of the wife). Table 1 shows compatible and incompatible combinations as described by Levins (1958).

TABLE I
Showing Compatible and Incompatible Combinations

| Incompatible Combination | | Compatible Combination | |
|--------------------------|---------|------------------------|---------|
| Wife | Husband | Wife | Husband |
| B | A | — | — |
| A | B | A | O |
| O | A | B | O |
| O | B | A B | O |
| O | A B | A B | A |
| — | — | A B | B |
| A | A B | B | B |
| — | — | A B | A B |
| — | — | O | O |
| B | A B | A | A |

Distribution of blood groups was studied in the couples and it was found that maximum number of husbands were of group A (48%) and blood group O was most commonly found in the wives (59.5%).

Number of cases of abortion encountered in different blood group females was also studied and it was found that the incidence of abortion was 54.5% in blood group O females, 20% in group A, 21.5% in group B and 4% in group AB females.

Estimation of antibody titre was carried out in the serum of 140 ABO incompatible females. The observations are as shown in Tables II & III, IVA IVB.

Table II shows anti B antibody titre in group A females. Eighteen cases were studied in this group. The maximum dilution found was 1:128 in 2 cases.

Table IVA & IVB show anti A anti B antibody titres in group O females. Total number of cases studied was 102 and the maximum dilution of anti A antibody

TABLE II
Showing Anti B Antibody Titre in Group A Females

| Blood Group | | Total No. of cases | Anti B Antibody titre in different dilutions | | | | | | | | | | |
|-------------|---------|--------------------|--|-----|-----|------|------|------|-------|-------|-------|--------|--------|
| Wife | Husband | | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1024 | 1:2048 |
| A | B | 12 | — | 1 | — | 3 | 2 | 4 | 2 | — | — | — | — |
| A | AB | 6 | — | — | — | 1 | 1 | 4 | — | — | — | — | — |

Table III shows anti A antibody titre in group A females. Total number of such cases studied was 20 and the maximum dilution encountered was 1:128 in only 1 case.

titre was 1:512 in 8 cases and maximum dilution of 1:512 of anti B antibody in 14 cases. Antibody titre was also studied in cases of control group. The maximum

TABLE III
Showing Anti A Antibody Titre in Group B Females

| Blood Group | | Total No. of cases | Anti A antibody titre in different dilutions | | | | | | | | | | |
|-------------|---------|--------------------|--|-----|-----|------|------|------|-------|-------|-------|--------|--------|
| Wife | Husband | | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1024 | 1:2048 |
| B | A | 15 | — | 2 | 2 | 4 | 2 | 4 | 1 | — | — | — | — |
| B | AB | 5 | — | 1 | — | — | 3 | 1 | — | — | — | — | — |

TABLE IV A
Showing Anti A Antibody Titre in Group O Females

| Blood Group | | Total No. of cases | Anti A antibody titre in different dilutions | | | | | | | | | | |
|-------------|---------|--------------------|--|-----|-----|------|------|------|-------|-------|-------|--------|--------|
| Wife | Husband | | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1024 | 1:2048 |
| O | A | 60 | — | — | 4 | 9 | 8 | 10 | 20 | 7 | 2 | — | — |
| O | B | 36 | — | 2 | 6 | 2 | 9 | 3 | 4 | 4 | 6 | — | — |
| O | AB | 6 | 1 | — | 1 | 1 | 2 | 1 | — | — | — | — | — |

TABLE IV B
Showing Anti B Antibody Titre in Group O Females

| Blood Group | | Total No. of cases | Anti B antibody titre in different dilutions | | | | | | | | | | |
|-------------|---------|--------------------|--|-----|-----|------|------|------|-------|-------|-------|--------|--------|
| Wife | Husband | | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1024 | 1:2048 |
| O | A | 60 | — | — | 4 | 10 | 7 | 16 | 12 | 5 | 6 | — | — |
| O | B | 36 | — | — | — | 4 | 5 | 7 | 4 | 8 | 8 | — | — |
| O | AB | 6 | — | 1 | 1 | — | 2 | 1 | 1 | — | — | — | — |

dilution encountered in the control group was only 1:128 in only one case.

Thus, from the above study of 200 cases of abortion and 55 cases of control group where antibody titre was estimated, one can conclude that antibodies could be found in higher dilutions in abortion cases as compared to control group of cases and comparatively a higher range of antibody dilutions was noted in group O females.

Discussion

Blood group distribution of couples of abortion and control group was studied and compared with the findings of other workers as shown in Table V.

less the same, but the over all incidence of group B in our cases under study of both abortion and control series, was higher as compared to the cases studied by Wren and Vos (1961) but they also did not find any significant difference in the incidence of group B in their abortion and control cases (vide Table V). The low incidence of group B encountered by Wren and Vos (1961) may be because of the fact that they observed that in a population which mainly included the white race the incidence of group B is comparatively low. High incidence of group O was a constant finding in wives of abortion series (59.5%) as compared to control cases (19%). Similar findings

TABLE V

Showing Distribution of Blood Groups in Couples of Control and Abortion Groups

| | | Total No. of cases | Blood groups in percent | | | |
|------------------------------|---------|--------------------------|-------------------------|------|------|-----|
| | | | A | B | O | AB |
| <i>Wren & Vos (1961)</i> | | | | | | |
| Control | Wife | 100 | 47 | 10 | 40 | 3 |
| group | Husband | | 35 | 11 | 51 | 3 |
| Abortion | Wife | 122 | 38 | 8 | 50 | 3 |
| group | Husband | | 45 | 9 | 41 | 2 |
| <i>Present series (1969)</i> | | | | | | |
| Control | Wife | 55 | 39 | 34.5 | 19 | 7.5 |
| group | Husband | | 30 | 31.5 | 32 | 6.5 |
| Abortion | Wife | 200 | 14.5 | 20 | 59.5 | 6 |
| group | Husband | | 48 | 26.5 | 15.5 | 10 |

The above table shows that the incidence of blood group A in this series mothers having abortion was lower (14.5%) than in control group (39%) Wren and Vos (1961), however, did not find any significant difference in the distribution of group A in mothers having abortion and in the control group.

The incidence of group B in both, the abortion and control series was more or

were also reported by Wren and Vos (Vide Table V).

Freda (1961) reported that the blood group factor of the foetus crosses the placental barrier and stimulates the antibody formation, which in its turn passes back to the foetus, thereby causing antigen-antibody reaction. This reaction can occur in utero at a very early stage and can result in abortion in early weeks of

gestation. Alpha and Beta haemolysins develop in group O mothers carrying group A, B or AB foetuses which explains a higher incidence of abortion in group O females (54.5%).

McNeil (1954) observed 45.1% incidence of abortion when the mother belonged to group O and father to group B, and about 50% out of these had two or more abortions.

Table VI compares the incidence of compatible and incompatible matings observed in cases of abortion by different authors. A striking difference was seen between incompatible and compatible combinations in the present study, 70% and 30%, respectively. Wren and Vos reported the incidence of compatible and incompatible combinations to be 55% and 45% respectively.

O mothers containing haemolysins in their sera.

The present series reveals a definitely higher incidence of abortions in ABO incompatible couples and more so when the wife belonged to group O. Kutcipal and Behrman (1963) studied 173 patients with the history of 3 or more abortions (not necessarily consecutive) and they could not establish any relationship between the blood groups of mother and foetus with the previous abortions. However, they did not refute the contention that blood group incompatibilities may be one of the aetiological factors in causing abortion.

It may therefore be concluded that the antibodies formed in the mother due to heterospecific pregnancy crossed the placental barrier and resulted in destruc-

TABLE VI

Showing Compatible and Incompatible Combinations Observed by Various Authors

| | Total No. of cases | Incompatible pregnancies in percent | Compatible pregnancies in percent |
|----------------------|--------------------|-------------------------------------|-----------------------------------|
| 1. Levine (1945) | 115 | 54 | 46 |
| 2. Mc.Neil (1954) | 85 | 57.6 | 42.4 |
| 3. Wren & Vos (1961) | 122 | 45 | 55 |
| 4. Present series | 200 | 70 | 30 |

Stratton (1955) suggested that the titre of anti A and anti B antibody rises during pregnancy in group O mothers irrespective of the foetus being group A or B. This signifies that potent haemolysins against foetal erythrocytes were present in the maternal sera. It cannot however be concluded from the foregoing that all pregnancies with incompatible matings will terminate prematurely or all the babies born will develop haemolytic disease due to ABO incompatibility. Perfectly normal babies have been born to group

tion of foetal red cells, thus causing death of the foetus. It can therefore be postulated that many cases of so called idiopathic spontaneous abortions can be attributed to maternal immunisation by dominant A or B agglutinogens.

Summary

The role of blood group incompatibility was studied in 200 couples where the wife aborted without any known aetiology. The findings were compared with 55 couples who did not have any abor-

tion. It was noted that 70% couples of the abortion group were ABO incompatible. In the abortion group, the incidence of group O females was as high as 59.5%, whereas it was 19% only in the wives of control series. The study of anti A and anti B antibody titres revealed that antibodies were present in maximum dilution in group O females, the maximum being 1:512 noted in 22 cases.

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