# IMPACT OF ABO BLOOD GROUPS ON THE FERTILITY OF DIFFERENT PARENTAL PAIRS

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## Abstract

Classical works dealing with the possibility of mother-child incompatibility with regard to basic ABO blood groups give contradictory conclusions (e.g. -(1,2)). Bioreproductive and population-genetic indicators have been studied in a sample of live births and in two pregnancy samples with different "a priori" and "a posteriori" risk assessment. The analysis points out that ABO blood groups can influence fertility of different parental pairs, and consequently - assessment of the individual pregnancy risk.

**Key words**: ABO blood groups, bioreproductive, population-genetics indicators.

## Introduction

There are various views, which are in conflict with each other, about clinical importance of immunity incompatibility mother-child with regard to belonging to basic blood groups of ABO system. Some authors think that this type of incompatibility has a reflection on fertility of different parental pairs (1,3), while the others have different conclusions (with certain reserve; (4,5). The manifestations of hemolytic anemia of newborns due to ABO incompatibility are generally mild and don't have big clinical importance (6). However, it is not possible to completely disregard the influence of belonging to ABO blood groups on complex immunity interaction between a mother and a child (2). It is very probable that these interactions could have influence on the level of risk of individual pregnancies, having in mind especially the occurrences in the early stages of pregnancy. In other words, the chances for successful pregnancy could depend on specific arrangement of parental pairs by blood groups of ABO system (7).

## Materials and methods

We want to show one attempt of usage of population-genetics analysis in order to contribute to the solution of this medical problem. Furthermore, in this paper the theoretical assumptions for possible detection of this controversial factor of fertility are being studied using population-genetics indicators. In the last few years the bioreproductive and population- genetics indicators have been analyzed in the samples of pregnant women, with a goal to determine the indicators of high risk for unsuccessful pregnancy. The basic population-genetics parameters of certain systems of group variations have been found earlier in observed groups (8, 9).

## Results and discussion

In accordance with the existing medical (immunity) theory, the parental pairs could be divided into two basic groups, and those are: risky parental pairs (by which can appear different symptoms of incompatibility) and not risky parental pairs. According to the same theory, the problems due to ABO incompatibility are threatening only to the mothers with the O blood group. This is followed by the conclusion that the fertility of corresponding pairs in population should be lower. On the other hand, the frequencies of reciprocal types of pairing in balanced population should be equal, by population-genetics theory (model of genetic balance). In other words, the appearance of ABO incompatibility should reflect in significant differences in frequency of critical and reciprocal types of pairing, and those differences should depend on the level of risk of different studied groups (samples of pregnancies). The well known theoretical basis of population-genetics analysis of basic groups of ABO system (10) are shown in Table 1.

In Table 2 the theoretical frequencies of critical types of pairing are shown, and those are the types of pairing which can result in ABO mother-child incompatibility.

Table 3. shows the studied samples, their symbols and sizes. It is shown a range of table data which is relevant for determining of statistical importance of differences in frequencies of critical and reciprocal types of pairing (tables 4-10) starting with previously calculated basic population-genetics parameters (9). In Table 6 reciprocal types are multiplied by reciprocal types (OxA, OxB, OxAB). In accordance with the model of genetic balance, the frequency of reciprocal types of pairing should be equal.

From the shown data (Tables 7, 8, 9) which is of descriptive character it is noticeable that this parameter is decreasing with the decrease of the prior estimate of the level of risk.

**Table 1.** The phenotype and genotype composition of balanced population with regard to the basic blood groups of ABO system.

| | BLOOD GROUP | | | | | |
|---|---|---|---|---|---|---|
| **Phenotype** | **A** | | **B** | | **AB** | **O** |
| **Genotype** | $I^AI^A$ | $I^AI^O$ | $I^BI^B$ | $I^BI^O$ | $I^AI^B$ | $I^OI^O$ |
| **Theoretical frequency** | $p^2$ | 2pr | $q^2$ | 2qr | 2pq | $r^2$ |
| | $p^2 + 2pr$ | | $q^2 + 2qr$ | | | |

**Table 2.** Critical types of pairing in population.

| Type of pairing | Total theoretical frequency | Theoretical frequency of risky pairs | Relative risk of individual pregnancy |
|---|---|---|---|
| AxO | $pr^2(p+2r)$ | $pr^2(p+r)$ | $p + r$ |
| BxO | $qr^2(q+2r)$ | $qr^2(q+r)$ | $q + r$ |
| ABxO | $2pqr^2$ | $2pqr^2$ | 1 |

**Table 3**. The size and the estimate of risk of studied samples.

| Studied samples | | Symbol | N | General prior estimate of the risk of studied pregnancies |
|---|---|---|---|---|
| Unsuccessful pregnancies (spontaneous miscarriages) | | E | 480 | +++ |
| Risky pregnancies (genetic advising) | Amniocentesis executed | A1 | 409 | ++ |
| | Amniocentesis not executed | A2 | 346 | + |
| Live births (Bui 1966) | | B | 265 | 0 |

**Table 4.** Proportion of genes $I^A$, $I^B$ and $I^O$ in studied samples.

| Sample | Gene proportions | | |
|---|---|---|---|
| | $pI^A$ | $qI^B$ | $rI^O$ |
| E | 0.24 | 0.12 | 0.64 |
| A1 | 0.29 | 0.14 | 0.57 |
| A2 | 0.37 | 0.17 | 0.46 |
| B | 0.28 | 0.13 | 0.59 |

Table 10. shows that the main part of the critical types of pairing are the pairings of the type AxO.

The expected frequencies were calculated from the corresponding population-genetics parameters (p,q, r), which are characteristic for each sample. In this Table the data for the samples A1 and A2 are merged into one record. It could be said that for this condensed record the general prior estimate of risk has conditional value of 1.5. As it could have been expected, the test shows that the samples are heterogeneous. This is understandable taking into consideration the fact that the samples are formed by strictly differential criteria of biological characteristics of pregnancy (unsuccessful pregnancies, risky pregnancies, successful pregnancies).

The obvious excess of critical and reciprocal types of pairing (with the exemption of normal pregnancies) has a very unequal statistical importance. As the Table shows, statistically the most important excess of reciprocal pairings is in sample E and sample A2.

Among the types of pairings (AxO, BxO, ABxO), whose fertility is endangered by ABO incompatibility mother-child, exists inequality in the level of risk. Furthermore, ABO incompatibility with the mother O exists among all the children of the pairing ABxO, while the level of risk

**Table 5.** Absolute frequencies of types of pairing.

| Type of pairing | Sample | | | |
|---|---|---|---|---|
| ♂x♀ | E | A1 | A2 | B |
| AxA | 26 | 62 | 54 | 41 |
| AxB | 18 | 9 | 24 | 16 |
| AxAB | 16 | 5 | 12 | 13 |
| AxO | 82 | 54 | 40 | 36 |
| BxA | 39 | 45 | 30 | 23 |
| BxB | 1 | 12 | 9 | 11 |
| BxAB | 7 | 6 | 11 | 3 |
| BxO | 41 | 26 | 8 | 6 |
| ABxA | 18 | 14 | 14 | 10 |
| ABxB | 8 | 7 | 6 | 4 |
| ABxAB | 0 | 4 | 6 | 2 |
| ABxO | 12 | 12 | 9 | 5 |
| OxA | 108 | 79 | 72 | 37 |
| OxB | 48 | 19 | 14 | 18 |
| OxAB | 25 | 9 | 7 | 4 |
| OxO | 31 | 36 | 30 | 36 |

**Table 6**. Absolute frequencies of critical and reciprocal types of pairing.

| Type of pairing | Critical | | | | Reciprocal | | | |
|---|---|---|---|---|---|---|---|---|
| | E | A1 | A2 | B | E | A1 | A2 | B |
| AxO | 82 | 54 | 40 | 36 | 108 | 79 | 72 | 37 |
| BxO | 41 | 26 | 8 | 6 | 48 | 19 | 14 | 18 |
| ABxO | 12 | 12 | 9 | 5 | 25 | 9 | 17 | 4 |
| $\Sigma$ | 135 | 92 | 57 | 47 | 181 | 107 | 103 | 59 |

**Table 7.** Theoretical proportions of critical types of pairing.

| Type of pairing | Theoretical proportion | Sample | | | |
|---|---|---|---|---|---|
| | | E | A1 | A2 | B |
| AxO | $pr^2(p+2r)$ | 0.149 | 0.135 | 0.101 | 0.142 |
| BxO | $qr^2(q+2r)$ | 0.069 | 0.058 | 0.039 | 0.059 |
| AbxO | $2pqr^2$ | 0.024 | 0.219 | 0.167 | 0.226 |
| | $\Sigma$ | 0.242 | 0.219 | 0.167 | 0.226 |

**Table 8.** Positive association between bcl-2 and PR expression*

| | | PR | | | | Total |
|---|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | |
| bcl-2 | 0 | 14 | 1 | 2 | 3 | 20 |
| | 1 | 3 | 2 | | 1 | 6 |
| | 2 | 2 | 3 | 1 | 4 | 10 |
| | 3 | 6 | 6 | 3 | 20 | 35 |
| Total | | 25 | 12 | 6 | 28 | 71 |

* Data are given as number (percentage of row total). P<0.001, linear-by-linear Association.

**Table 9.** Cox regression test results

| | B | SE | Wald | df | Sig. | Exp(B) |
|---|---|---|---|---|---|---|
| **GRADE** | -.123 | .628 | .039 | 1 | .844 | .884 |
| **ER** | .004 | .005 | .624 | 1 | .430 | 1.004 |
| **PR** | -.006 | .006 | 1.144 | 1 | .285 | .994 |
| **Bcl-2** | -.029 | .014 | 4.181 | 1 | .041 | .972 |
| **THERAPY** | -.213 | .114 | 3.529 | 1 | .060 | .808 |
| **LNS*** | .815 | .379 | 4.627 | 1 | .031 | 2.260 |
| **SIZE** | 1.675 | .821 | 4.161 | 1 | .041 | 5.341 |

LNS-Lymph node status

**Table 10.** Percentage of critical types of pairing in relation to the total number of cases of critical types of pairing.

| Type of pairing | Sample | | | |
|---|---|---|---|---|
| | E | A1 | A2 | B |
| AxO | 60.74 | 58.69 | 70.17 | 76.60 |
| BxO | 30.37 | 28.26 | 14.04 | 12.77 |
| ABxO | 8.89 | 13.04 | 15.79 | 10.64 |

of incompatibility for other "critical" pairs differs (Table 13) and it depends from population-genetics parameters (incompatibility can appear only in half of heterozygote fathers of A and B blood group, and participation of heterozygote in population and all its parts has a theoretical value of 2pr or 2qr). The risk is equal to the possibility of heterozygosis of the father.

These differences are not taken into consideration in showed analysis.

## Conclusion

It should be mentioned that these findings do not give completely unified conclusions in terms of presence or absence of ABO incompatibility mother-child, or conclusions about the value of population-genetics analysis for detection of the consequences of such incompatibilities. The analysis of frequency of critical and reciprocal parental pairs confirms the thesis that the belonging to ABO blood groups plays a certain role in complex immunity interactions between mother and the child. In other words, it can have an effect on the estimate of the risk of pregnancy.

**Table 11.** Test of homogeneousness of samples (11) with the regard to the frequency of studied types of pairing. (* Table is in the text with the original data).

| Estimate of the risk | Sample | T8* e | T6* $o_{crit}$ | T6* $o_{rec}$ | $(o_{crit}-e)^2$ | $(o_{rec}-e)^2$ | $(o_{crit}-e)^2/e$ | $(o_{rec}-e)^2/e$ | $\sum[(o-e)^2/e]$ | df |
|---|---|---|---|---|---|---|---|---|---|---|
| 2 | E | 116.1 | 135 | 181 | 357.21 | 4212.01 | 3.08 | 36.28 | 39.36 | 1 |
| 1 | A | 147.2 | 149 | 210 | 3.24 | 62.80 | 0.02 | 0.43 | 0.45 | 1 |
| 0 | B | 59.8 | 47 | 59 | 163.84 | 0.64 | 2.74 | 0.01 | 2.75 | 1 |
| Pool. | | | | | | | | | 42.56 | 3 |
| tot. | | 323.1 | 331 | 450 | 62.41 | 16103.61 | 0.19 | 49.84 | 50.03 | 1 |
| dif. | | | | | | | | | **7.47** | 2 |

**Table 12.** Statistical importance of deviation of the frequency of critical and reciprocal types of pairing from their expected frequency calculated from population - genetics parameters.

| Sample | Crit | Rec | theor | $\chi^2$crit-theor | p | $\chi^2$rec-theor | p |
|---|---|---|---|---|---|---|---|
| E | 135 | 181 | 116.1 | 3.08 | >.25 | 36.28 | <.005 |
| A1 | 92 | 107 | 89.5 | 0.07 | >.25 | 3.42 | >.25 |
| A2 | 57 | 93 | 57.7 | 0.01 | >.25 | 21.60 | <.005 |
| B | 47 | 59 | 59.8 | 2.74 | >.25 | 0.01 | >.25 |

**Table 13.** Relative risk of appearance ABO incompatibility mother-child in critical types of pairings.

| | The possibility of heterozygosis of the father | | | |
|---|---|---|---|---|
| | E | A1 | A2 | B |
| AxO | 0.84 | 0.80 | 0.714 | 0.81 |
| BxO | 0.91 | 0.89 | 0.84 | 0.90 |
| AbxO | 1.00 | 1.00 | 1.00 | 1.00 |

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