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# ABO-Hp Interaction and Unexplained Infertility

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After Ritter and Hinkelmann, Kirk and his Colleagues Kirk also reported that in matings where the father is in-compatible with the mother with respect to the ABO groups, the children show a higher frequency of the $Hp^1$ gene. The possible explanation was that $Hp^1$ gene is more efficient than $Hp^2$ in, removing dissolved haemoglobin from the plasma and conserving the contained iron and hence in cases where foetuses or children are affected by haemolytic disease due to foetal A or B inherited from the father, one who is of type $Hp^{1-1}$ should have the best, and one who is $Hp^{2-2}$ the worst, chance of survival. However, because Haemolytic disease of the new born due to anti-A or anti-B is rarely fatal, at was later recognized Kirk that the iron conservation theory was unlikely to be correct. In another study by Vana and Steinberg, it was reported that haptoglobin-ABO interaction is not clearly related to ABO incompatibility but suggested to study the relationship between ABO and haptoglobin phenotypes directly.

The present study has been conducted on the couples with absolute inability to produce children having a married life span of more than two years even when both the partners were otherwise found normal and fit to produce children. These couples have been labeled as "unexplained" infertility cases, in the light of American Fertility Society and Marshall which state that a couple is considered infertile when pregnancy has not occurred after a year of coitus without usage of any family limiting methods.

The main objective of the present study is to reveal if ABO-Hp association costs and also is it a contributing factor towards infertility or childlessness of the couple.

## Material and methods

A total number of 250 couples visiting outdoors of Gynaecology Department of Govt. Medical College, and Mata Kaushalaya Hospital, Patiala screened by senior Gynaecologists and urologists form the data base of the study. Data on 100 normal fertile couples having two or more children with no history of abortion or still birth from the same population has been used as control group Kaur.

The couples screened were cases of unexplained infertility since no evident reason could be assigned for their infertility. These couples had a married life span of two or more years (32.4% couples had a married life span ranging from 2 to 4 years and the mean married life span was 8.06 years) and were having normal sexual life. The physical examination of both the partners was done so as to rule out any associated pathology hampering their reproductive performance. Routine biochemical tests were carried out on the couple. In addition semenology of the husband followed by endometrial biopsy tubal patency tests of wife to rule out the abnormalities if any of spermatozoa or ovulation respectively. Only those couples were selected in which all these tests were found normal for the present study.

ABO blood grouping was done according to the standard techniques of Dunsford and Bowley. The technique of horizontal starch gel electrophoresis was used for the study of haptoglobin phenotypes 11 present hydrolyzed starch (Sigma made) was used for making the gel. Electrophoresis was conducted in the discontinuous buffer, system Poulik.

**Results and Discussion**

Table 1 depicts the phenotypic and gene frequencies of ABO blood groups among fertile control group and infertile couples. In both the groups, B blood group predominates (37.50 and 38.20 percent respectively) followed by O, A and AB. Frequency of gene 'r' is maximum (.548 in control and .555 in infertile couples). Statistically insignificant differences have been found in the infertile and control group and also amongst the husband and wives of the two groups.

**Table 1:** Distribution of ABO blood groups among infertile and fertile groups

| Group | Category | No. tested | Blood Group | | | | Gene frequency | | | Probability d.f. = 3 |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | O | A | B | AB | p | q | r | |
| **Infertile** | H | 250 | 84 | 53 | 90 | 23 | | | | |
| | W | 250 | 70 | 52 | 101 | 27 | | | | |
| | Total | 500 (100.0) | 154 (30.80) | 105 (21.0) | 191 (38.20) | 50 (10.0) | 0.1647 | 0.2757 | 0.5550 | .70>P<.50 |
| **Fertile** | H | 100 | 33 | 20 | 38 | 9 | | | | |
| | W | 100 | 27 | 27 | 37 | 9 | | | | .70>P<.50 |
| | Total | 200 | 60 (30.0) | 47 (23.5) | 75 (37.5) | 18 (9.00) | 0.1837 | 0.2739 | 0.5477 | .90>P<.80 |

Table 2 gives the break up of Hp types and gene, frequencies in the two groups. In both the groups maximum number is of Hp2-2 type, 55.00 in the control and 59.80 percent in the infertile group, followed by 2-1 and 1-1 type. $Hp^2$ gene has a higher frequency compared to $Hp^1$ gene in fertile (.2400) as well as infertile (.2050).

**Table 2:** Distribution of Hp Types among infertile and fertile groups

| Group | Category | No. tested | Hp group | | | Gene frequency | | Probability |
|---|---|---|---|---|---|---|---|---|
| | | | 1-1 | 2-1 | 2-2 | $Hp^1$ | $Hp^2$ | |
| **Infertile group** | H | 250 | 3 | 96 | 151 | | | .70 > P < .50 |
| | W | 250 | 1 | 101 | 148 | | | |
| | Total | 400 (100.0) | 4 (0.80) | 197 (39.40) | 299 (59.80) | .2050 | .7950 | |
| **Fertile group** | H | 100 | 3 | 3 | 64 | | | .05 > P < .02 |
| | W | 100 | 3 | 51 | 46 | | | |
| | Total | 200 (100.0) | 6 (3.0) | 84 (42.00) | 110 (55.00) | .2400 | .7600 | .10 > P < .05 |

The distribution of' various Hp types in the four blood groups among infertile individuals is showing statistically, insignificant differences (Table 3). Similar picture is observed from values on fertile individuals for ABO and Hp parameters (Table 4), indicating no association between these two factors.

**Table 3:** Distribution of Hp Types in ABO blood groups among infertile individuals

| Blood group | Haptoglobin types | | | Total | Gene frequency | |
|---|---|---|---|---|---|---|
| | Hp1-1 | Hp2-1 | Hp2-2 | | Hp1 | Hp2 |
| **A** | 2 (1.90) | 40 (38.10) | 63 (60.0) | 105 (21.00) | .2095 | .7905 |
| **B** | 1 (0.52) | 84 (43.98) | 106 (55.50) | 191 (38.20) | .2251 | .7749 |
| **AB** | 0 - | 23 (46.00) | 27 (54.00) | 50 (10.00) | .2300 | .7700 |
| **O** | 1 (0.65) | 50 (32.47) | 103 (66.88) | 154 (30.80) | .16688 | .8311 |
| **Total** | 4 (0.80) | 197 (39.40) | 299 (59.80) | 500 (100.00) | | |
| **$X^2$ = 11.8198; d.f. = 6, .10 > P .05.** | | | | | | |

**Table 4:** Distribution of Hp types in the ABO blood groups among fertile individuals

| Hp1 | Hp2 | ABO blood group | Haptoglobin | | | Total |
|---|---|---|---|---|---|---|
| | | | Hp 1-1 | Hp 2-1 | Hp 2-2 | |
| .2447 | .7553 | A | 1 (2.13) | 21 (44.68) | 25 (53.19) | 47 (23.50) |
| .23995 | .75995 | B | 1 (1.33) | 34 (45.33) | 40 (53.33) | 75 (37.50) |
| .2775 | .72225 | AB | 2 (11.11) | 6 (33.33) | 10 (55.56) | 18 (9.00) |
| .22495 | .77495 | O | 2 (3.33) | 23 (38.33) | 35 (58.33) | 60 (30.00) |
| | | Total | 6 (3.00) | 84 (42.00) | 110 (55.00) | 200 (100.00) |
| **d.f. = 6; $X^2$ = 4.3528; .70>P<.50** | | | | | | |

When the frequencies of the genes $Hp_1$ and $HP_2$ are calculated in various ABO blood groups among the two population groups, it is observed that in the control sample (Table 4) frequency of $Hp_1$ gene is highest in blood group A B (0.2778) followed by blood group A, B and least in blood group O (0.2250). In the infertility group (Table 3) the $Hp_1$ gene is highest in AB (.2300) followed by B (.2251), A (.2095) and O (.1688). This trend is in conformity with the observations made by Vana and Steinberg (1975), who have concluded that there is a tendency, which they cannot at present explain, for, $Hp_1$, frequencies to increase with blood group in order O, A, B, AB. In the control sample however, only blood groups A and B interchange their places, and rest of the trend being the same.

The most prevalent Hp mating type is 2-2 x 2-2 followed by 2-1 X 2-1, 2-2 X 2-1 and 2-1 X 2-2. The other matings 1-1 X 2-2, 1-1 x 2-1 and 2-2 X 1-1 are occurring in few couples. In the infertile group no couple was found group maximum number of couples had 2-2 x 2-1 mating followed by 2-2 X 2-2 and 2-1 X 2-2. The mating types 2-1 X 2- 1, l-1 X 2-1 and 2-1 X 1-1 are having very less number of couples. No couple was found for mating types 1-1 X 1-1, 1-1 X 2-2 and 2-2 X 1-1. In the ABO compatible matings, in the control group B X B type is most frequent whereas in the infertile couples O X B mating is most prevalent (Table 5).

**Table 5:** Distribution of infertile and fertile couples according to possible haptoglobin combinations in ABO compatible matings

| ABO mating type (H x W) | Total No. of couples | Hp mating type (H x W) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1-1 x 2-1 | 1-1 x 2-2 | 2-1 x 1-1 | 2-1 x 2-1 | 2-1 x 2-2 | 2-2 x 2-1 | 2-2 x 2-1 | 2-2 x 2-2 |
| **A x A** | 10<br>(5) | 0 | 2<br>(0) | 0 | 2<br>0 | 2<br>(2) | 0 | 2<br>(1) | 2<br>(2) |
| **B x B** | 33<br>(12) | 0 | 0 | 0 | 9<br>2 | 9<br>(2) | 1<br>(0) | 4<br>(7) | 10<br>(1) |
| **B x AB** | 12<br>(4) | 0 | 0 | 0 | 1<br>(0) | 4<br>(0) | 0 | 5<br>(3) | 2<br>(1) |
| **A x AB** | 2<br>(1) | 0 | 0 | | 0<br>(1) | | | 1 | 1<br>(0) |
| **O x AB** | 9<br>(4) | 0 | 0 | 0<br>(2) | 1<br>(0) | 0 | 0 | 2 | 6<br>(2) |
| **O x A** | 21<br>(8) | 1<br>(1) | 0 | 0 | 8<br>(0) | 3<br>(1) | 0 | 6<br>(2) | 3<br>(4) |
| **O x B** | 38<br>(11) | 0<br>(1) | 0 | 0 | 6<br>(0) | 10<br>(3) | 0 | 6<br>(3) | 16<br>(4) |
| **AB x AB** | 4<br>(0) | | | | 3<br>(0) | | | | 1<br>(0) |
| **O x O** | 16<br>(10) | | | | 2<br>(1) | | | 4<br>(3) | 10<br>(4) |
| **Total** | 145<br>(55) | 1<br>(2) | 2<br>(0) | 0<br>(2) | 32<br>(4) | 28<br>(10) | 1<br>(0) | 30<br>(19) | 51<br>(18) |

* No mating was found with 1-1 x 1-1 combination.

** Figures in parentheses are for normal fertile couple.

Similarly in ABO incompatible matings, the distribution of Hp mating types is showing a prevalence of 2-2 X 2-2 mating type in infertile group, followed by 2-2 X 2-1, 2-1 x 2-2 and 2-1 X 2-1. No couple was found with mating type 1-1 X 1-1, 1-1 X 2-1, 1-1 X 2-2, 2-1 X 1-1 and 2-2 X 1-1. In the fertile group maximum number of couples are with 2-2 X 2-1. Mating type followed by 2-1 X 2-2, 2-2 X 2-2 and 2-1 X 2- 1. The mating types 1-1 X 2-1 and 2-2 X 1-1 have only 1 couple each. No couple was found with 1-1 X 1-1, 1-1 X 2-2 and 2-1 x 1-1. Out of the ABO incompatible matings, the most frequent matings were B X O and B X A in the infertile and fertile groups respectively (Table 6).

**Table 6:** Distribution of infertile and fertile couples according to possible haptoglobin combinations in ABO incompatible matings

| ABO mating type H x W | Total couples | 1-1 x 2-1 | 2-1 x 2-1 | 2-1 x 2-2 | 2-2 x 1-1 | 2-2 x 2-1 | 2-2 x 2-2 |
|---|---|---|---|---|---|---|---|
| **A x B** | 24 | 0 | 4 | 2 | 0 | 14 | 4 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | (9)** | | (2) | (2) | | (4) | (1) |
| **B x A** | 14<br>(112) | 0 | 4<br>(1) | 4<br>(3) | 0<br>(1) | 0<br>(5) | 6<br>(2) |
| **AB x B** | 6<br>(5) | - | 1<br>(10) | 0<br>(1) | - | 0<br>(3) | 5<br>(1) |
| **AB x A** | 7<br>(2) | 0 | 1<br>(0) | 2<br>(0) | - | 0<br>(1) | 4<br>(1) |
| **AB x O** | 6<br>(2) | - | 1<br>(1) | 2<br>(0) | 0<br>- | 0<br>- | 3<br>(1) |
| **A x O** | 17<br>(5) | - | 3<br>(1) | 3<br>(2) | - | 4<br>(2) | 7<br>(0) |
| **B x O** | 31<br>(10) | 0<br>(1) | 2<br>(1) | 7<br>(3) | - | 4<br>(4) | 18<br>(1) |
| **Total** | 105<br>(45) | 0<br>(1) | 16<br>(6) | 20<br>(11) | 0<br>(1) | 22<br>(19) | 47<br>(7) |

* No mating was found with 1-1 x 1-1, 1-1 x 2-2 and 2-1 x 1-1 combinations.

** Figures in parentheses are for fertile couples.

The data on ABO compatible/incompatible matings have been pooled up for similar/dissimilar status for Hp types of the husband and the wife in the infertile and fertile groups (Table 7). The value of chi-square is showing non-significant results. But when the ABO compatible and incompatible matings are taken separately for Hp similar/dissimilar status of husband and wife, we are getting statistically significant results (Table 8) indicating an association between the two i.e. the Hp similar/dissimilar status amongst the ABO compatible as well as ABO incompatible.

**Table 7:** ABO compatible/incompatible matings and the Hp similar/dissimilar status among the infertile and fertile groups

| **Group** | **Mating type** | **Total No. of couples** | **Similar** | **Dissimilar** | **$X^2$** | **d.f.** | **Results** |
|---|---|---|---|---|---|---|---|
| **Infertile** | Compatible | 145 | 83 | 62 | 0.211 | 1 | Non-significant |
| | Incompatible | 105 | 63 | 42 | - | - | - |
| **Fertile** | Compatible | 55 | 22 | 33 | 1.35 | 1 | Non-significant |
| | Incompatible | 45 | 13 | 32 | - | - | - |

**Table 8:** ABO compatible/incompatible matings and the Hp similar/dissimilar status among the infertile and fertile groups

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Mating type Compatible** | Infertile | 145 | 83 | 62 | 4.79 | 1 | Significant |
| **Incompatible** | Fertile | 105 | 63 | 42 | | | |
| **Compatible** | Infertile | 55 | 22 | 33 | 12.50 | 1 | Significant |
| **Incompatible** | Fertile | 45 | 13 | 32 | | | |

**References**


1. American Fertility Society 1971. How to organize a basic study of the infertile couple Birmingham, U.S.A.: American Fertility Society.

2. B Ananthakrihnan, R., W. Beck, H. Walter, A. Arandt Hauser, W. Gumble, H. Leithoff, R. Wigand. W. Zimmermann & B. Boros 1973. A mother-child combination analysis for ABO-Bp interaction. Humangenetik, 18: 203-206.

3. Dunsford, I & C. C. Bowley 1967. Techniques of blood grouping. London: Oliver Boyd, Edinburgh.

4. Kaur, S. 1983. Genetic markers and sex ratio. M. Phil. thesis, Punjabi University, Patiala (Unpublished).

5. Kirk, R. L., H. Kinns & N. E. Morton 1970. Interaction between the ABO blood group and haptoglobin sytem. Amer J. Hum. Genet., 22: 384-389.

6. Kirk, 1971. A haptoglobin mating frequency, segregation and ABO blood group interaction analysis for additional series of families. Ann. Hum. Genet., 34: 329-337.

7. Marshall, J. R. 1978. Infertility in current obstetric Gynaecologic Diagnosis Treatment by Beason Ralph, C. Large, Los Altos, California, United Publications.

8. Poulik, M. D. 1957. Starch gel electrophoresis in a discontinuous system of buffers, Nature 180: 1477.

9. Ritter, H. & K. Hinkelmann 1966. c.f. Genetic Markers in Human Blood by E. R. Gilbelt, Oxford and Edinburgh: Blackwell Scientific Publications.

10. Vana, G. & A. G. Steinberg 1975. Haptogtobin ABO interaction, a possible explanation for excess of $Hp^1$ among the offspring of ABO incompatible rnatings. Amer. J. Hum. Genet., 27: 224.

The study is pledged to throw discernible light on the nature of existence of ABO-Hp association and whether it is a contributing factor towards infertility of the couple. In as doing it examines 250 couples, visiting outdoors of the Gynecology Departments of two Medical Colleges at Patiala. The data reveal various interesting facets of interaction and infertility.