

ABO blood groups and *Leishmania donovani chagasi* infection: an apparent association

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ABSTRACT

A relatively large sample derived from an endemic area of visceral leishmaniasis, showed a significant association between *Leishmania donovani chagasi* infection and the group A phenotype of the ABO blood group system. A joint analysis of the present data with those of the literature, showed a highly significant and apparently consistent association between these two traits.

INTRODUCTION

Decker-Jackson and Honigberg (1978) showed, through sensitive immunological techniques, the existence of cross reactions between the antigens of the ABO blood groups system and some surface antigens of *Leishmania*. On the basis of these results, a "mimicry" mechanism employed by the parasite to evade the host's immune response was suggested (Greenblatt *et al.*, 1981). Specific studies directed to test this hypothesis have provided contradictory results (Evans *et al.*, 1984; Amendoeira *et al.*, 1987).

The ABO blood groups of a sample from an endemic area were determined and compared with similar samples to test the suggested association.

MATERIAL AND METHODS

The general data refers to a total of 1604 individuals belonging to 243 nuclear families from Jacobina (Bahia State), Brazil, an endemic area for Visceral Leishmaniasis (Lima *et al.*, 1984a). The analysis was performed on a sub-sample of about 600 individuals, for which data on immunological tests to detect the infection were available.

The characterization of infection was made through clinical data, anamnesis, intradermic reaction against *L. donovani chagasi* antigens and serological analysis (Reed *et al.*, 1986; Badaró *et al.*, 1990).

Among the infected individuals, there were 21 cases of Kalazar, 18 confirmed by medular puncture, while the remaining three cases were based only on anamnesis.

Data on 13 polymorphic genetic systems (ABO, phosphoglucomutase 1, glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, adenylate kinase, glyoxalate, esterase D, carbonic anhydrase II, glutamic-pyruvate transaminase, acid phosphatase, adenosine deaminase, haptoglobin and hemoglobin) were used to remove family inconsistencies (illegitimate children).

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Skin tests were made by an intradermal injection of 50 µg of soluble protein obtained by freeze-thaw preparations of *L. donovani chagasi* centrifuged at 35,000 x g. The micro-enzyme-linked immunosorbent assay was performed with a soluble antigen of *L. donovani chagasi* - WR strain (Bahia), read in a spectrophotometer with a 405 nm filter. This technique was able to discriminate the sera from chagasic patients from those infected by Leishmanias in mixed endemic areas (Badaró *et al.*, 1990).

The phenotype determination for the ABO system was made, by the classical indirect technique, on sera stored at -40°C against a panel of A and B red blood cells. This determination was made by two different people and a third test performed when inconsistency was detected.

Woolf's statistical test was applied, in order to determine relative risks, and infer on both significance and heterogeneity (Woolf, 1955).

RESULTS AND DISCUSSION

Table I shows the contingency analysis of A blood group x non-A blood group individuals. As can be seen, only the filial generations showed a significant increase of relative risk of A individuals, although the parental generation did show a similar, however, non-significant, relative risk. The pooled analyses showed a significant increase of risk of A individuals, without signs of heterogeneity.

The joint analysis of the present sample and those from two other endemic areas of Brazil did show

Table I - Comparison between ABO blood group A and non-A individuals infected or not with *Leishmania donovani chagasi*, in Jacobina, Brazil.

| Samples | VL group | Infected | | Non infected | | Relative risk | χ^2 | |
|-------------------|----------|----------|-------|--------------|-------|---------------|----------|------------------|
| | | A | Non-A | A | Non-A | | | |
| Jacobina (Parent) | | 29 | 46 | 26 | 71 | 1.712 | 2.738 | 0.005 < P < 0.10 |
| Jacobina (Child) | | 34 | 59 | 73 | 213 | 1.684 | 4.285 | 0.02 < P < 0.05 |
| Total | | 63 | 105 | 99 | 284 | 1.695 | 7.021 | P < 0.01 |

| Heterogeneity analysis | | | |
|------------------------|----|----------|-----------------|
| Source | df | χ^2 | |
| Total | 4 | 7.023 | 0.10 < P < 0.25 |
| Significance | 1 | 7.021 | P < 0.01 |
| Heterogeneity | 3 | 0.002 | P > 0.99 |

Table II - General analysis of blood group A risk toward *Leishmania donovani chagasi* infection.

| Samples | VL group | Infected | | Non infected | | Relative risk | χ^2 | |
|--------------------------------|----------|----------|-------|--------------|-------|---------------|----------|-----------------|
| | | A | Non-A | A | Non-A | | | |
| Jacobina (Parent) ¹ | | 29 | 46 | 26 | 71 | 1.712 | 2.738 | 0.05 < P < 0.10 |
| Jacobina (Child) ¹ | | 34 | 59 | 73 | 213 | 1.684 | 4.285 | 0.02 < P < 0.05 |
| Teresina ² | | 51 | 72 | 34 | 111 | 2.296 | 9.806 | P < 0.005 |
| Ceara ³ | | 25 | 51 | 431 | 944 | 1.084 | 0.106 | 0.50 < P < 0.75 |
| Total | | 139 | 228 | 564 | 1339 | 1.606 | 12.516 | P < 0.001 |

| Heterogeneity analysis | | | |
|------------------------|----|----------|-----------------|
| Source | df | χ^2 | |
| Total | 4 | 16.935 | P < 0.005 |
| Significance | 1 | 12.516 | P < 0.001 |
| Heterogeneity | 3 | 4.419 | 0.10 < P < 0.25 |

¹Present study; ²Amendoeira *et al.*, 1987; ³Evans *et al.*, 1984.

a highly significant increase of relative risk among A individuals and no significant heterogeneity (Table II).

These results show that there is, in fact, an average increase of relative risk (1.7, on average) of A individuals as compared with non-A controls. Racial and/or social stratification could influence this association. Nevertheless, at least for the filial generation sub-sample of the present material, no such explanation can be attached to the data, since the non-affected individuals are sibs of the affected subjects. Moreover, better racial markers than the ABO system did not show any association with *L. donovani chagasi* infection, in the same sample (Lima *et al.*, 1984b).

Although these results strongly suggest a real association between these two traits, a study of cutaneous leishmaniasis showed no such association, suggesting either other types of host response and/or behavior associated with the ABO polymorphism or a particular antigenic difference between these *Leishmania* species (Esteree and Dedet, 1989).

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RESUMO

Uma amostra relativamente grande obtida em uma área endêmica de leishmaniose visceral mostrou uma significativa associação entre o fenótipo A do sistema sanguíneo ABO e a infecção por *Leishmania donovani chagasi*. A análise conjunta dos presentes dados e aquelas obtidas da literatura mostraram uma altamente significativa e aparentemente consistente associação entre essas duas características.

REFERENCES

- Amendoeira, M.R.R., Cabello, P.H., Krieger, H., Kalil, J. and Marzochi, M.C.A.** (1987). Association of *Leishmania donovani* infection and ABO blood groups. *Mem. Inst. Oswaldo Cruz, 82 (suppl): 78.*
- Badaró, R., Pedral-Sampaio, D., Johnson Jr., W.D. and Reed, S.G.** (1990). Evaluation of the stability of a soluble intradermal skin test antigen preparation in American visceral leishmaniasis. *Trans. Roy. Soc. Trop. Med. Hyg. 84: 226-227.*
- Decker-Jackson, J.E. and Honigberg, B.M.** (1978). Glycoproteins released by *Leishmania donovani*. Immunological relationships with host and bacterial antigens and preliminary biochemical analysis. *J. Protozool. 25: 514-525.*
- Esteree, P. and Dedet, J.P.** (1989). The relationship of blood group type to American cutaneous leishmaniasis. *Ann. Trop. Med. Parasitol. 83: 345-348.*
- Evans, T., Talapala, G.N., Alencar, J.E. and Pearson, R.D.** (1984). The relationship of american visceral leishmaniasis to ABO blood group type. *Ann. J. Trop. Med. Hyg. 33: 805-807.*
- Greenblatt, C.L., Kark, J.D., Schnur, L.F. and Slutzky, G.M.** (1981). Do *Leishmania* serotypes mimic human blood group as antigens? *Lancet I: 505-506.*
- Lima, A.M.D., Azevedo, E.S., Souza, M.G., Eulálio, M.C., Reed, S.G., Badaró, R., Jones, T.C., Cabello, P.H. and Krieger, H.** (1984a). A distribuição familiar da infecção por *L. donovani* em Jacobina (BA). *Proceedings of the XI Reunião Anual sobre Pesquisa Básica em Doença de Chagas (Caxambú, MG), pp. 55.*
- Lima, A.M.D., Melo, C.A., Eulálio, M.C., Reed, S.G., Abreu, M.C.A., Nogueira, C.P., Mestriner, M.A., Cabello, P.H. and Krieger, H.** (1984b). Um estudo de associação entre 12 marcadores genéticos sanguíneos e as formas de infecção por *L. donovani*, em Jacobina (BA). *Proceedings of the XI Reunião Anual sobre Pesquisa Básica em Doença de Chagas (Caxambú, MG), pp. 56.*
- Reed, S.G., Badaró, R., Masur, H., Carvalho, E.M., Lourenço, R., Lisboa, A., Teixeira, R.S., Johnson Jr., W.D. and Jones, T.C.** (1986). Selection of a skin test antigen for american visceral leishmaniasis. *Am. J. Trop. Med. Hyg. 35: 79-85.*
- Wolf, B.** (1955). On estimating the relation between blood group and disease. *Ann. Hum. Genet. 19: 251-253.*

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