

FREQUENCY OF HLA-B27 ANTIGEN IN IRANIAN PATIENTS WITH BRUCELLOSIS AND IT'S RELATIONSHIP WITH OSTEOARTICULAR COMPLICATION

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ABSTRACT

Objectives: To determine frequency of HLA-B27 in brucellosis patients and to investigate a possible association between osteoarticular brucellosis and HLA-B27 antigen.

Methodology: Sixty patients with serologically confirmed brucellosis and 100 healthy controls were screened for HLA-B27 by using standard microlymphocytotoxicity method. Osteoarticular involvement was suggested by clinical presentation and confirmed by nuclear scan. Patients were placed in two groups and compared, patients with osteoarticular involvement (OAP group) and without osteoarticular involvement (OAN group). All data were analyzed by SPSS (version 11.5, USA) and using Fisher's exact X2 test.

Results: Out of total 60 patients with brucellosis 38 (63.3%) were male. Mean age of the patients were 36.2±12.3 with the range of 18-65 years. HLA-B27 test was positive in 11 patients (18.33%) with brucellosis, whereas in control group HLA-B27 positivity was 7% (p<0.05). The prevalence of HLA-B27 in OAP and OAN groups was 33.33% and 8.33%, respectively (p<0.05).

Conclusions: The prevalence of HLA-B27 in our brucellosis patients is higher than normal population and there is a significant association between HLA-B27 and brucellar osteoarthritis in the region of study.

KEYWORDS: Brucellosis, Osteoarticular involvement, HLA-B27, Ahwaz.

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INTRODUCTION

Brucellosis is a zoonosis that produces severe morbidity in humans, and, is still of both health and economic significance in many developing countries.¹ The disease exists worldwide, especially in the Mediterranean basin, the Arabian Peninsula, the Indian subcontinent, in parts of Mexico and Central and South America.² The prevalence of brucellosis is 60 to 80/100,000 in Mediterranean and most Middle Eastern countries. Iran has a disease incidence of 132/100000.^{3,4} Among the clinical manifestations of brucellosis, arthritis may occur in over one-third of the patients.²

Different articular syndromes have been well recognized: some are definitely infectious in nature, whereas others appear to be reactive.⁵

The possibility that B27 antigens could predispose to the occurrence of brucellar spondyloarthritis was investigated in previous studies with controversial results. Hodinka et al reported a positive relationship between possession of HLA-B27 and spondyloarthritis in chronic brucellosis. However, Alarcon et al found no increased incidence of any HLA type in their patients with acute brucellosis induced arthritis compared with cases of brucellosis without arthritis.^{5,6} Ertema et al⁷ reported that although HLA-B27 frequency in brucellosis patients with osteoarticular involvement was slightly higher than patients without osteoarticular involvement, but, there was no significant difference ($p > 0.05$). Because of high prevalence of brucellosis cases in Iran and as no published Iranian study of HLA antigens in brucellosis case could be found, we decided to conduct the study.

The aim of the present study was to determine frequency of HLA-B27 in brucellosis patients and to investigate a possible association between osteoarticular involvement of brucellosis and HLA-B27 antigen.

METHODOLOGY

This prospective analytic descriptive study was carried out in 60 patients, in infectious diseases ward of Razi Hospital in Ahwaz south west Iran, during 2003-2006. Following inclusion criteria for brucellosis were considered 1) Clinical features 2) Positive serology according to Iranian national program against brucellosis (Wright 1:80 or more, two mercaptoethanole (2ME) 1:40 or more, Comb's Wright >1:80) or positive blood or bone marrow cultures. Inclusion criteria for definite diagnosis of osteoarticular involvement were 1) Clinical features, not explained by other diseases, 2) abnormal nuclear bone scan. Standard microlymphocytotoxicity technique method was used for detection of HLA-B27 antigen in 60 patients with brucellosis and 100 healthy controls (normal blood donors). A questionnaire including characteristic demographic and brucellosis related factors were used to collect data. Patients with brucellosis were placed in two groups and compared with each other. Patients with osteoarticular involvement as OAP group and patients without osteoarticular involvement as OAN group. All data were analyzed by SPSS (version 11.5, USA) and using Fisher's exact X2 test.

Table-I: Demographics of patients with brucellosis and osteoarticular syndrome in Ahwaz, Iran

| Variables | | Brucellosis n(%) | Osteoarticular brucellosis n(%) | P value |
|------------|---------------|------------------|---------------------------------|---------|
| Age(year) | <25 | 11 (18.3) | 5 (20.8) | 0.53 |
| | 25-45 | 24 (40) | 10 (41.7) | |
| | 46-65 | 19 (31.7) | 9 (37.5) | |
| | >65 | 6 (10) | 0 (0.0) | |
| Gender | Male | 38(63.33) | 16(66.66) | 0.48 |
| | Female | 22(36.67) | 8(33.34) | |
| Occupation | High exposure | 41(68.33) | 13(54.16) | 0.16 |
| | Low exposure | 19(31.67) | 11(45.84) | |
| Residency | Rural area | 35(58.33) | 14(58.33) | 0.59 |
| | Urban area | 25(41.67) | 10(41.67) | |
| Total | | 60(100) | 24(100) | |

SD; standard deviation

RESULTS

Out of total 60 patients with brucellosis 38(63.3%) were male and 22(36.7%) were female. Mean age of the patients were 36.2 ± 12.3 (mean \pm SD) years with the range of 18-65 years. Demographic data in brucellosis patients and osteoarticular involvement are shown in Table-I. There was no significant difference in age, gender, residency and risk of occupational exposure between two groups ($p > 0.05$). HLA-B27 test was positive in 11 patients (18.33%) with brucellosis, whereas in control group HLA-B27 positivity was 7%. The results of HLA-B27 test in patients with and without osteoarticular involvement are shown in Table-II. The overall prevalence of HLA-B27 in the study population (160 subjects 60 with brucellosis & 100 controls) was 11.25%. There was significant difference in HLA-B27 positivity between two groups ($p < 0.05$) and between brucellosis patients and controls ($p < 0.05$).

DISCUSSION

Brucellosis like other chronic inflammatory conditions such as ankylosing spondylitis is associated with HLA B27. But the association is not absolute.⁸ In the present study the prevalence of HLA-B27 in brucellosis patients was higher than normal population (blood donor as control group), with the rate of 18.33% vs. 7%, respectively. This finding is consistent with some previous studies^{6,7,9} but, also in consistent with other studies.^{5,10} Paeja et al, in their work did not find an HLA-B27 increase in the group

of patients with brucellosis associated spondylarthritis when compared with healthy individuals.¹⁰ Alarcon, et al reported that. HLA-B27 frequency was diminished in the Peruvian brucellosis patients. The most interesting finding was the presence of a statistically significant low frequency of HLA-A2 in the disease group suggesting that this antigen may play a protective role for the development of brucellosis.⁵ We believe that geographical differences, difference in strain of *Brucella* (*Abortus* vs. *Melitensis*) and genetic factors other than HLA-B27 may play a role in these differences. Dawes et al, reported that *B. abortus* is different of *B. melitensis* in relation to HLA antigens.⁹

Our study revealed significant association between HLA-B27 and osteoarticular involvement in brucellosis patients. This finding is similar to only with few previous studies.⁶ Most of the published studies discarded a significant association between HLA-B27 and osteoarticular brucellosis.^{5,7,9,10} The reason for this finding is not clear for us but, chronic illness in our osteoarticular patients (most of them had positive two ME suggesting brucellosis with more than one year duration) may be responsible for this difference.

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Table-II: HLA-B27 positivity in brucellosis patients with or without osteoarticular involvement in Ahwaz, Iran

| Group | HLA-B27 positive n(%) | HLA-B27 negative n(%) | Total | P value |
|----------------------|-----------------------|-----------------------|-------|---------|
| Brucellosis patients | 11(18.33) | 49(81.67) | 60 | 0.03 |
| Controls | 7(7) | 93(93) | 100 | |
| Total | 18 / 160 (11.25%) | 142 / 160 (88.75%) | 160 | |
| OAP | 8(33.33) | 16(66.67) | 24 | 0.01 |
| OAN | 3(8.33) | 33(91.67) | 36 | |
| Total | 11 | 49 | 60 | |

OAP = Brucellosis patients with osteoarticular involvement, OAN = Brucellosis patients without osteoarticular involvement, percent are in parentheses

Conflict of interest: There is no conflict of interest.

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