

Association of HLA (Class I & II) and Susceptibility to Hydatid Cyst Disease

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Summary:

Background: Hydatid cyst disease is a parasitic zoonotic disease caused by genus *Echinococcus*. This disease believed to has genetic background in it's aetiopathogenesis course .

The aim of this study is to shed light on the possible correlation between HLA-class I (A,B,C) & HLA-class II (DR & DQ) antigens and the susceptibility to this disease.

Patients & Methods: Fifty patient with hydatid cyst disease before undergoing surgical operation were investigated for HLA. Class I and class II by using microlymphocytotoxicity test. The results were compared with 115 healthy control.

Results: Significant increased trend of HLA-A₂₈ and A₁₁, -B₁₈ and B₃₅, -DR₃ and DR₁₁ ($P < 0.001$, $P < 0.01$) in patients with this disease as compared with healthy control. On the other hand, increased trend of HLA-A₂₈ ($P < 0.01$) in patients with hydatid disease especially in those with a cyst location in liver.

Conclusions: High frequency of HLA-A₁₁ and -A₂₈, B₁₈ and -B₃₅, -DR₃ and -DR₁₁ antigens may play major role in susceptibility to hydatid disease. HLA-A₂₈ could be the most related antigen to this disease and acting as genetic marker that could in one way or another play crucial role in susceptibility especially in cases of hydatid disease in liver.

Keywords: Hydatid cyst disease, HLA-typing

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Introduction

Hydatid cyst disease is a parasitic zoonotic disease the aetiology of this disease is the genus of platyhelminthes worms called *Echinococcus* especially the two important species which are *E. granulosus* and *E. multilocularis*.¹

Genetic background contribute to its aetiopathogenesis (genetic predisposition) represented by human leukocytes antigens (HLA), both class I & class II which increase susceptibility and decrease or modify immune response against this disease.^{2,3,4}

This study was designed to assessing the frequency of HLA antigens (class I & II) in association with disease susceptibility to such disease in sporadic cases and to elucidate the role of genetic factor in the pathogenesis of this disease in Iraqi patients.

Patients & Methods

A total of 50 Iraqi Arab patients with hydatid cyst disease before undergoing surgery (36 female, 14 male) were included in this study, who were attending the surgery department in the

Specialist Hospital of Disease of Liver and Gastrointestinal System and Specialist Surgeries Hospital at Baghdad Medical City in Baghdad and Baquaba General Hospital from Dec. 2004 – Sep. 2005.

Data cover detailed comparisons among sex, age and ethnic matched 115 healthy control.

Typing for HLA class I (A,B,C) and class II (DR, DQ) antigens was carried out by using microlymphocytotoxicity established by Terasaki (1964), and modified by Dick & Bender (1984) with wide range of specific antisera (59 antigens of class I and 21 antigens of class II).

Statistical analysis

The association between HLA antigens and the disease was evaluated in terms of relative risk (RR), etiological fraction (EF), and preventive fraction (PF), While the statistical differences were assessed by Fisher exact probability test (probability – p- and probability with correction – Pc-).

Results

The frequency of HLA class I and II which give significant difference between the two study groups as illustrated in table 1, an increased trend of A₁₁, A₂₈ antigens (RR=3.67, EF=0.2, $P < 0.01$, $P_c < 0.05$), (RR=13.04, EF=0.51, $P < 0.001$, $P_c < 0.001$) respectively.

Significant increase in B₁₈, B₃₅ antigens in patients group (RR=7.26, EF=0.27, $P < 0.001$,

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Pc<0.001) as compared with control group (RR=10.03, EF=0.41, P<0.001, Pc<0.001), table 1.

Also significant increase in DR3, DR11 antigens in patients in comparison to control group (RR=3.95, EF=0.41, P<0.001, Pc<0.01), (RR=27.03, EF=0.4, P<0.001, Pc<0.001) respectively, table 1.

Non significant difference was found in DQ antigens (P>0.05) in patients group as compared with healthy control group.

On the other hand, significant correlation between HLA and the site of hydatid cyst is shown in table 2, especially HLA-A₂₈ which show significant deviation (P<0.01) in correlation with the site of hydatid cyst in liver.

Table 1: Comparison in phenotype of HLA antigens which give significant differences between the study groups

HLA antigen	Patients with hydatid cyst disease Vs. healthy control						
	Patients No. (%)	Control No. (%)	RR	EF	PF	P<	Pc<
HLA-A							
11	14(28)	11(9.56)	3.67	0.2	-	0.01	0.00
28	29(58)	15(13.04)	9.2	0.51	-	0.001	0.00
HLA-B							
18	16(32)	7(6.08)	7.26	0.27	-	0.001	0.00
35	23(46)	9(7.82)	10.03	0.41	-	0.001	0.00
HLA-DR							
3	28(56)	28(24.34)	3.95	0.41	-	0.001	0.00
11	21(42)	6(5.21)	27.03	0.4	-	0.001	0.00

RR= relative Risk, EF=Etiological fraction, PF= Preventive fraction, P= Probability, Pc=Probability with correction

Table 2: HLA antigens which give significant difference with site of hydatid cyst

HLA antigen	RR	EF	PF	X ² y	P*	Pc**
A ₂₈	3.156	0.541	-	4.868	0.007	0.203

* P<0.01
 ** Pc>0.05

Discussion

Many studies reported abroad have mentioned that there is a strong association between HLA-antigens both classes (I & II) and susceptibility to hydatid cyst disease.^{3,4,5,6,7,8,9,10} The phenomenon of immunological or constitutional resistance may be dependent upon a potential immunogenetic predisposition with a potential HLA association.³

Significant increase in frequency of A₁₁, A₂₈, B₁₈, B₃₅, DR₃ & DR₁₁ haplotypes in patients

group providing evidence that these antigens play crucial role in susceptibility to this disease coincide with previous world wide studies. Furthermore HLA₂₈ has the highest frequency in this study and could be considered as a genetic marker for aetiopathogenesis of hydatid disease in Iraqi Arab patients especially in those with cyst located in liver.

The presence of different HLA antigens among different studies of other societies and our study may be due to ethnic differences among world population and/or could be due to small sample of patients taken in this study, or could be due to mirage among ethnic groups of Iraqi Society from very previous generations.

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