Effect of HLA-B27 on Development of Psoriatic Arthropathy

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ABSTRACT

Background: Psoriatic arthritis is a type of arthritis that can often affect some patients who suffer from psoriasis. Approximately 40-50% of individuals with psoriatic arthritis have the HLA-B27 genotype

Objective: To investigate whether we could confirm the role of HLA-B27 alleles and psoriatic arthritis in Iraqi Arab Muslims patients.

Method: A cross sectional case control comparative study included thirty Iraqi Arab Muslims who had psoriatic arthritis that consulted the Dermatological and Rheumatological Department in AL-Kindy Teaching Hospital from November 2014 to June 2015. HLA-genotyping for HLA-B27 were assessed. A control group consisted of fifty-one healthy volunteers among the staff of Al-Kindy College of Medicine that did not have psoriatic arthritis or family history of psoriasis. HLA-B*27allele was done by using an Exicycler TM 96 Real-time Quantitative Thermal Block (Bioneer, Daejeon, Korea) and Accupower, HLA-B27 real-time PCR kit (Bioneer, Daejeon , Korea)

Results: Plaque type psoriasis is more common than other types of psoriasis (66% versus 34%). There is no association between psoriatic arthritis and HLA-B27 with p-value of 0.1197 and Odds ratio (confidence interval) of 2.9375 (0.755-11.415).

Conclusions: HLA B*27 is not associated with psoriatic arthritis in Iraqi Arab Muslims patients.

Key words: psoriatic arthritis, HLA-B*27, PCR.

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INTRODUCTION

Psoriatic arthritis is a long – term inflammatory arthritis that occur in people affected by the autoimmune disease psoriasis. The classic feature of psoriatic arthritis is swelling of entire fingers and toes with a sausage-like appearance [1, 2].

This often happens in association with changes to the nail such as small depressions in the nail (pitting), thickening of the nails, and detachment of the nail from the nail bed, skin changes consistent with psoriasis (e.g red scaly and itchy plaques) [3].

Psoriatic arthritis affects up to 30% of people with psoriasis and occurs in both children and adults. The exact cause of psoriatic arthritis is not yet known, but genetic factors are thought to be strongly involved in the development of psoriatic arthritis. The more recent genome – wide association studies provide further evidence of genetic heterogeneity, although modest in size, they do suggest links between key factors in the immune responses both locally in the skin and also systemically implicating both innate and adaptive immunity [4, 5]. Obesity and

certain forms of psoriasis are thought to increase the risk. Approximately 40-50% of individuals with psoriatic arthritis have the HLA-B27 genotype [3,6,7] . In Iraq, as to our Knowledge, no published study for the association between HLA B*27and psoriatic arthritis. This study is designed to show the association between HLA B*27 and psoriatic arthritis.

METHODS

The study consisted from Iraqi Arab Muslims patients suspected to have psoriatic arthritis consulted the Dermatological and Rheumatological Department in Al-kindy Teaching Hospital in Baghdad from November 2014 to June 2015. Healthy controls are the staff of Al-Kindy College of Medicine. The study took place at the HLA-Typing Research Unit, Al-Kindy College of Medicine, University of Baghdad.

The Scientific and Ethical Committee of AL-Kindy College of Medicine approved

the study and all samples were obtained with informed consent in accordance with the AL-kindy Teaching Hospital declaration.

Blood samples have been obtained from both patients and control and genomic DNA was extracted using reliaprep spin column kit (promega, USA). Real-time PCR reactions were performed using an Exicycler TM 96 Real-time quantitative thermal block (bioneer, Daejeon, korea) and the accu power, HLA-B27 real – time PCR kit (Bioneer,Daejeon, Korea).

The following 2 detection probes were used: an HLA B27-specific probe and aglyceraldehyde-3-phosphate dihydrogen-ase (GAPDH) – specific probe, which were labeled with a fluorescent reporter dye FAM (6-carboxy fluorescein) and TAMRA (6-carboxy tetramethyl - rhodamine) at the 5 end respectively and a fluorescent quencher dye BHQ (Black hole quencher) at the 3' end , for both.

The real – time PCR reaction was performed in atotal volume of 50ml with the HLA-B27 pre-mix (Bioneer, Daejeon, Korea), which contains HLA-B27-specific primers targeting exon 2 of HLA-B gene, GAPDH specific primers, dual –labeled fluorogenic probes, DNA polymerase, deoxynucleotide triphosphates (DNTPS), and stabilizer, with 5ml of template DNA and 45 ml of 0.1% diethyl pyrocarbonate-treated distilled water. The amplification protocol for this reaction consisted of an initial denaturation step at 95Cº for 5min, followed by 35 amplification cycles of denaturation for 5sec at 95Cº, annealing and extension for 15sec at 65Cº.

During the PCR, the HLA-B27 target region and an internal control region for GAPDH were amplified simultaneously. Fluorescence signals were monitored in real – time to determine the threshold cycle number (Ct).

A cut – off value was assigned on the basis of Ct values for FAM and TAMRA reporter dyes to interpret the results.

Specimens yielding Ct FAM value of <30 and a Ct TAMRA value of <27 were interpreted as being HLA-B27 positive. Samples yielding a Ct FAM value of >30 were considered HLA-B27 negative. If the internal control signal was above the assigned cut- Off (Ct TAMRA<27). A sample was considered to contain inhibitory substances or degraded DNA, if the Ct TAMRA value was> 27. HLA-B27 positive and negative controls were coamplified.

Statistical Analysis: Was done using MiniTab version 13. P-value less than 0.05 was considered positive. Odds ratio and 95 % confidence interval were measured.

RESULTS

Thirty patients with psoriatic arthritis are involved in this study with fifty-one healthy controls. The age of the patients in this study were ranged from 8 to 55 with a mean (20.4± 14.17) while Age of controls range from 21 to 45 with a mean (37±9.3) as shown in Table 1.

Plaque type psoriasis forms about 66% from psoriatic cases as with 6 cases are positive for HLA-B27 allele. While the control group, 3 (6%) are positive for HLAB27as shown in table 2 and 3.

Table 4 shows that positive cases for B27 have no significant association regarding joint manifestation.

Table (1): Age and gender for both patient and control group.

		Patient group	Mean ± SD	Control group	Mean±SD
Age		8-55	20.4 ±14.17	21-45	37±9.3
Gender	**Male**	18		29	
	Female	12		21	

Table (2): HLAB27 in both patient and control group

Group	HLA B27 Positive	HLAB27 Negative	Odds Ratio (95%C.I)	P-value
Patient	6	24	2.94 (0.75-11.42)	0.1197
Control	4	47		

Table (3): Psoriasis type and HLA B27 allele frequency

	Plaque type No. (%)	Other type No. (%)	Odds ratio (C.I)	P-Value
Type of psoriasis	20 (66)	10 (34)		
B27 Positive	4 (20)	2 (20)	1 (0.14-6.67)	1
B27 Negative	16 (80)	8 (80)		

Table(4): Association between HLA B27 and joint manifestation.

	HLA B27 positive	HLA B27 negative	Odds ratio (95%C.I)	P-value
Hands and wrist arthritis	3	10	1.4 (0.23-8.4216)	0.7132
Elbow	2	7	1.2 (0.1794-8.2171)	0.8422
Knee	1	5	0.76 (0.07-8.06)	0.81
Feet, ankle arthritis	0	2	N.A	

DISCUSION

In this study, there was no association between HLA-B27 and psoriatic arthritis.
A study in Iraq revealed that HLA- C12, C17, DRB1 07 and DQB1 02 alleles may be as a risk factors associated with psoriasis, while HLA-C 04 and HLA-DQB1 alleles as protective factors [8]
Some studies showed that HLA-B16, B17, B27 and cw6 were associated with psoriatic arthritis in Caucasians[9] and HLA-A2, B46, DR8 and B27 were associated with psoriatic arthritis in Japanese[10]. Another study from china showed that HLA-B27 and Cw12 was associated with psoriatic arthritis[11]. Data from North – America presents HLA-B27 positively in 10 to 25% of patients with psoriatic arthritis and 90% in ankylosing spondylitis[12]. In north Spain, HLA-B27 is found in 8.8% of the population. It is estimated that 17% of patients with psoriatic arthritis in this region are positive for this antigen[13], also the study correlates the HLA B27 allele with different diseases, and the conclusion was that northern spain population shows higher level of B27 diversity than other Caucasian groups. In Brazil, it was 20.6% positive of patient with psoriatic arthritis [14] On the other side, other study found that HLA-B27 was negative in 32 of the 44 Brazilian patients (72.7%), and there was no association between HLAB27 and psoriatic arthritis[15] as this is approved in our study.
From above studies, the association between B27 and psoriatic arthritis is not fully elucidated although most of the studies show positive correlation between psoriatic arthritis and HLA B*27.
The explanation of discrepancies between the result of this study and other studies may be due to ethnicity, racial background, sample size of patient and control groups. Another explanation of the result is that patients in this study was complaining from peripheral rather than axial disease as HLAB*38, HLAB*39 (which are not investigated in this study) are increased among those with peripheral polyarthritis while HLA B*27 is common in those with axial disease [16,17]. All the above causes served as a source of bias.
We recommended further study with larger sample and studying the frequency of HLA B*27 in Iraqi population.

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