Associations of specific HLA-c loci and sociodemographic factors with the prevalence of type I psoriasis in Iraqi patients

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ABSTRACT

Psoriasis is an autoimmune inflammatory disease of human skin with the etiology being unknown and for which there is no cure. It is believed to be genetically and immunologically conditioned and has major negative impact on life's quality. This study aims to determine the impact of inheritance of specific human leukocyte Antigen-C loci and some sociodemographic factors on the susceptibility to early onset psoriasis (Type I). Current study includes psoriatic group involve 76 patients (type I) and a match apparently healthy group comprise 87 persons as a control. A polymerase chain reaction based method (low resolution sequence specific primer) used to detect C*06, C*07 and C*17 allele after inform consent. Current study shows that the C*06 and C*07 allele significantly associated with early onset psoriasis (p-value < 0.05), while C*17 shows no significant association. There is also higher percentage of patient were in urban (84.2%) than rural resident (15.8%). with no significant association between smoking and type I psoriasis (p-value >0.05). Both of C*06 and C*07 genotypes increase the risk of early onset psoriasis. While rural residency decreases the chance of getting type I psoriasis. Furthermore, lack of association with smoking cannot mitigate the effect of passive smoking.

Keywords: C*06; C*07; C*17; Psoriasis; Residency; Smoking; Type I.

INTRODUCTION

Psoriasis defined as a common, chronic disease, with a genetic basis, it characterized by an inflammation and proliferation activity [1]. Typically, psoriasis lesions characterized by erythematous papules which develop to form plaques that characterized by sharp borders and increased scaling [2]. It has a complex, multifactorial nature that influenced by genetic, environmental factors and immune components, with a worldwide prevalence of approximately 1 to 3% [3]. According to age of onset, Psoriasis characterized by bimodal distribution. (Type I) early onset psoriasis and (Type II) late onset psoriasis [4]. Other authors, identify type I psoriasis as inherited and associated with Cw6, while type II psoriasis occurs sporadically [5]. Several susceptibility loci have been identified, among them, PSORS1 (6p21.3) is a well-confirmed, in which HLA-Cw6 is the main marker allele, and have been notified in a number of studies [6]. susceptibility to psoriasis in different ethnic groups is associated with different HLA alleles [5]. This study aims to determine the impact of inheritance of specific HLA-C loci including C*06, C*07 and C*17, and some sociodemographic factors on the susceptibility to early onset psoriasis (Type I).

MATERIALS & METHODS

This is a prospective case control study comprised seventy-six patients diagnosed by dermatologist, selected from those visited the dermatological clinic in al-Zahra teaching hospital in al- kut city from February to august 2017, based on the age of first attach (been less than 40 years) of chronic plaque psoriasis. And a match eighty-seven apparently healthy persons as a control. Informed consent was obtained before venous blood sample (2 ml) toke from each patients and controls in K3-EDTA anticoagulated tube and subjected to a DNA extraction procedure. After that, the extracted DNA that fulfil the required purity and concentration aliquot and stored at -20c° for polymerase chain reaction amplification and detection. A PCR-SSP based technique used in current study with the primer sequence shown in table (1). In current study a primer with specific sequence for glyceraldehyde 3 phosphate dehydrogenase (GAPDH) used as a control primer. The obtained result shown in figure (1):

Results

The mean age for patients is 26.2 years. The male and female frequencies not highly differ in psoriatic patients, accounting about 47.4% to 52.6%. About 84.2% of psoriatic patients' resident in an urban location while only 15.8% with rural residency. All data about demographic traits of participant shown in table (2). About 16% of patients found to be smoker, and about 42% of relatives to some psoriatic patients also smoke. In compare to 26% smoker in non-relative group. A statistical significance differences was found between patients and relative groups (p-value < 0.05) table (3). About 18% of psoriatic patients show the presence of C*06 allele. in compared to about 8% and 1% in relatives and non-relatives respectively. A statistical significance differences found between patient and non-relatives (p-value < 0.05). according to this results, C*06 increase the risk of psoriasis eleven times (OR 11.3). The C*07 allele detected in 26% of patients, and in lower percentage in both relatives (11%) and non-relatives (5%). C*07 increase the risk of psoriasis about five times (OR 5.7). statistical significance differences found between patients versus relatives and patients versus non-relatives. for C*17, there is none statistical significance difference found neither between patients and relatives nor between patients and non-relatives (p-value > 0.05). C*17 allele detected in 31%, 38% and 29% in patients, relatives and non-relatives respectively. As shown in table (4).

Discussion

Psoriasis is a chronic, multisystem inflammatory disease, affects both sexes equally, the Pathogenesis is multifactorial, and has a bimodal age of onset [7]. early onset psoriasis accounting about 75% of patients and occurs before the age of 40 years, Patients have a strong family history and the Majority of them are CW6 positives. late onset psoriasis (type II) presents after the age of 40 years, Patients have no family history and are Cw6 negative [8].

Current study found a higher percentage of patient were in urban than rural resident. Little are the study that focus on psoriasis prevalence in association with residency, Salah and Bassam., 2012 [9] found that about three quarters of psoriatic patients reside city in Iraq while the rest inhabitants of rural areas or immigrated to urban areas recently. Two explanations for this finding can be suppose. First, urban social and physical environment (e.g. traffic noise) contributing to increased stress [10].

Second, skin microbiota alteration in psoriasis also associated with residency, based on The facts that the skin microbiota resembles those in soil, and as the immune function in later life depend on the early cross-talk between the developing immune system and microbiota [11]. This can lead to the hygiene hypothesis which postulate that reduction in microbial exposure in urban area due to improved sanitary can promoting autoimmune disease development. In contrast to rural area were microbes specially helminth in close contact. Immune regulatory properties of microbes from environment, especially helminthes led to their therapeutic application of several immune-mediated conditions including psoriasis based on experimental models and clinical studies [12].

lower percentage of patients was smoker compare to relatives and non-relatives group. The association between psoriasis and smoking is bidirectional, with the entrance of stress as third party, this relation become more complex. Making a triangle with reversible effect with each other's. smoking can be risky for psoriasis both psychologically and physiologically. While smoker do smoke to mitigate stress, smoking itself can cause stress [13]. Furthermore, although a proven relation between smoking and both prevalence and severity of psoriasis has been existed, patient with psoriasis had a higher tendency to smoking [14]. In Iraq, Khalifa et al., 2009 [15] found that the smoker had earlier age of onset, more chronic disease and less response to treatment, while Ata et al., 2003 [16] found a significant association with smoking prior to the onset of the disease while no significant association after the onset of psoriasis. The discrepancy of current finding with several studies that showed an association between smoking and psoriasis [17], [18] can be easily solved because about 35% of patients in this study below 20 years and female make 52% of total patients for which smoking is prohibited in Iraq. On the other hands about 16% of patients are active smoker while about 42% of relative are smoker make high percentage of patients a passive smoker (second hand smoker). Smoking induce oxidative stress and free radical production, increased secretion of IL2, IL12, TNF and IFNγ, and abnormal angiogenesis [19]. Free radical production during smoking activate signaling pathways implicated in psoriasis, such as nuclear factor kB, while smoking byproduct (nicotine) activate T cell to produce IL17 and IL22 major cytokines involved in the psoriasis pathogenesis [20]. Smoking also increases the level of IL-1, IL-6 and TNF-α while decreases the levels IL-10 [21]. Passive smoking as equal as active smoking risks, and can cause serious diseases in infants and children, with female were more likely to be exposed [22], [23].

In current study, the C*06 allele significantly associated with psoriasis patients than apparently healthy non relative control. C*07 also significantly associated with psoriasis. While C*17 shows no significant association with psoriasis. These three HLA type make the mainstay of this study. the frequencies of C*06 antigen in Iraqi Arab Muslims and Kurd Muslims about 2%, while C*07 20% in Arab versus 9% in Kurd [24]. Another study found that from 13 different HLA-C alleles in Iraqi Kurd seven alleles had frequencies higher than 4% including HLA C*06, C*07 and C*017 [25]. Ahmed., 2008 [26] in his survey about HLA typing in UC patients in Iraq, detect C*06 and C*07 in 12% and 18% of healthy control respectively. Several studies conducted in Iraq that investigate the association of HLA types with psoriasis. Batool., 2013 [27] identified C*07 among others as risk allele for psoriasis. Ahmed., 2016 [5] revealed that C*17 (but not C*06 or C*07) among others were significantly associated with psoriasis in Iraqi patients. In Neighboring Countries, a study about childhood psoriasis in Kuwait by Nanda et al., 2000 [28] showed a significant association with C*01. C*06 significantly increases in frequency in the type I patients compared with controls in Turkish [29]. C*06 allele although no statistically significant, increased in type I psoriatic patients than controls in Omanis [30]. The global association of C*06 allele with PSO have been validated with different population, including South Asians [31], and East Asians [32], Europeans [33]. and Egyptian [6]. The importance of C*06 allele associated with psoriasis is not only about its role in presenting autoantigen to T-cell. C*06 positive patients tend to develop extensive and sever disease, while C*06 negative patients suffer from dystrophic nail changes and PSA [34]. HLA-C*06-positive psoriatic responded quickly to ustekinumab with almost 90% improvement within 4 weeks, compared to 60% of HLA-C*06 negative patients [35]. C*06 allele may offer protection from PSA [36].

Conclusions and Recommendations

In conclusion, this study showed that the C*06 and C*07 allele are associated with early onset psoriasis. While the inheritance of C*17 is equal for patients and healthy subject. There is also decrease in frequency of psoriasis in rural area, which indicate that the earlier encounter with foreign environment the butter development of immune system. And finally, avoidance of indoor smoking is crucial for precaution from psoriasis specially when there is a positive family history.

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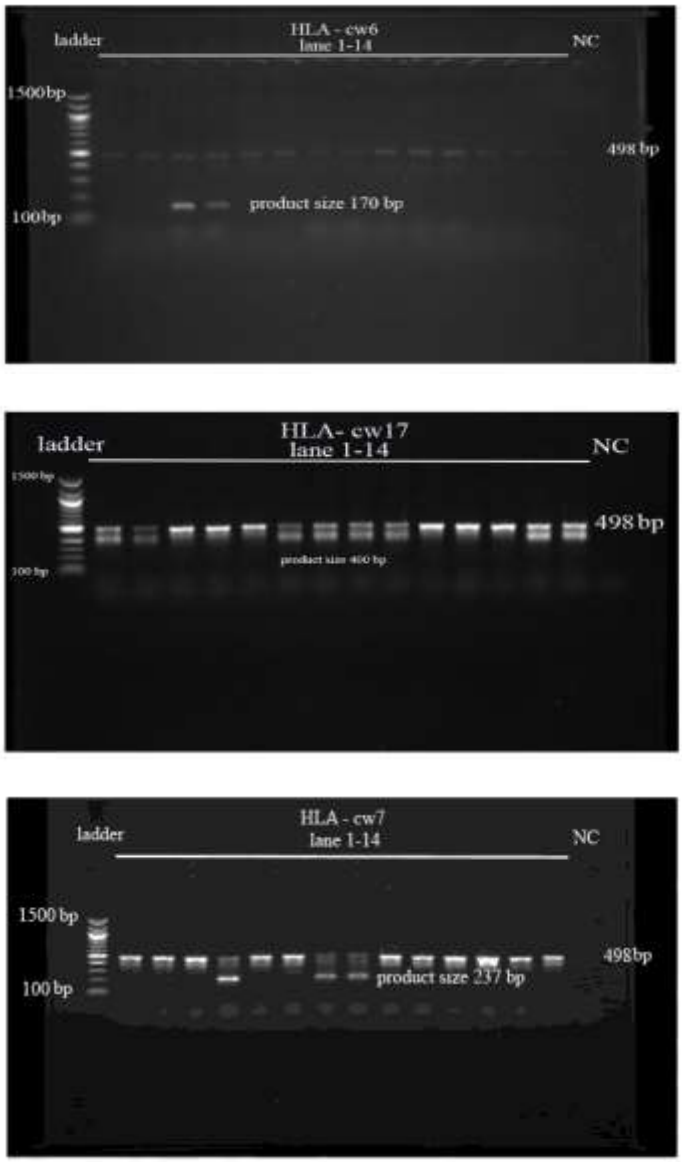

Figure 1: Gel electrophoresis results. each band identified by comparing with corresponding band of molecular ladder.

Table 1: Primers sequence employed in this study.

No.	Target	Sequence 5'-3'	Product size	References
1	HLA-cw6 F	GGATCAGGACGAAGTCCCAG	170 bp	NCBI/ primer-BLAST
2	HLA-cw6 R	GGGGACGCGTCATGAGTATT		
3	HLA-cw7 F	TTA CAT CGC CCT GAA CGA GG	237 bp	NCBI/ primer-BLAST
4	HLA-cw7 R	GGC CAT CCC GGG AGA TCT AT		
5	HLA-cw17 F	GGA TGA GGG GTC ATG TGT CT	400 bp	NCBI/ primer-BLAST
6	HLA-cw17 R	AGT AAG TGC TGG CAC ACA GG		
7	GAPDH F	AGA CCA CAG TCC ATG CCA TC	498 bp	NCBI/ primer-BLAST
8	GAPDH R	CAG GGC CCT TTT CTT GAG CC		

Table 2: Distribution of patients and control according to gender and residency.

Study sample				
	Patients n=76	Controls n=87	Total n=163	P- value*
Gender (no.) %				
Male	(36) 47.4	(43) 49.4	(79) 48.5	0.458
Female	(40) 52.6	(44) 50.6	(84) 51.5	
Residency (no.) %				
Urban	(64) 84.2	(81) 97.2	(145) 89.0	0.06
Rural	(12) 15.8	(6) 2.8	(18) 11.0	

Table 3: Distribution of patients and controls according to smoking behavior.

Sample	Smoking behavior			
	Smoker (no.) %	Nonsmoker (no.) %	*OR	**Sig.
Patients (Pts.) n=76	(12) 15.8	(64) 84.2	Pts. vs. NR 0.5	0.1
Relatives(Rel.) n=36	(15) 41.7	(21) 58.3	Pts. vs. Rel 0.2	0.003
Nonrelatives(NR.)	(13) 25.5	(38) 74.5		
Total n=163				
* Odds Ratio, Chi-square test, **p-value				

Table 4: Frequency of HLA-c allele among patients and control.

C*06	Present (no.)%	Absent (no.)%	*OR	**Sig
Patients n=76	(14) 18.4	(62) 81.6	Pts. vs. NR 11.3	0.002
Relatives n=36	(3) 8.3	(33) 91.7	Pts. vs. Rel 2.5	0.1
Non-relatives n=51	(1) 1.96	(50) 98.03		
Total n=163				

C*07	Present (no.)%	Absent (no.)%	*OR	**Sig
Patients n=76	(20) 26.3	(56) 73.7	Pts. vs. NR 5.7	0.002
Relatives n=36	(4) 11.1	(32) 88.9	Pts. vs. Rel 2.8	0.05
Non relatives n=51	(3) 5.9	(48) 94.1		
Total n=163				

C*17	Present (no.) %	Absent (no.) %	*OR	**Sig
Patients (Pts.) n=76	(24) 31.6	(52) 68.4	Pts. vs. NR 1.1	0.5
Relatives (Rel.)	(14) 38.9	(22) 61.1	Pts. vs. Rel. 0.7	0.3
Non relatives n=51	(15) 29.4	(36) 70.6		
Total n=163				
* Odds Ratio, Chi-square test, **p-value				