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Association between HLA-C*06 and Psoriasis in Bangladeshi Population

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Abstract **Original Research Article**

Background: Psoriasis is a T-cell driven inflammatory skin disorder which has a complex genetic background. Till date >86 psoriasis susceptibility loci have located, among which HLA-C*06 is the most strongly associated with a global prevalence ranging from 10.5% to 77.2% in psoriatic patients. Carriers of HLA-C*06 have distinct clinical phenotype with an early onset, worse disease progression but less chance of developing psoriatic arthritis and cardiovascular comorbidities. Moreover, better response with methotrexate and certain biologics are noted in HLA-C*06 carrier patients. This study aims to evaluate frequency of HLA-C susceptible alleles in psoriatic patients and in normal population by PCR and to observe the association of HLAC 06 with age of onset, gender, BMI, pattern & severity of psoriasis by statistical analysis. ***Methods:*** This study took place in the department of Dermatology and Venereology department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh over a period from July 2021 to June 2022 In total 40 psoriasis (diagnosed based on history, clinical symptoms, and/or histological report) along with 40 apparently healthy controls fulfilling the inclusion and exclusion criteria were enrolled following consecutive sampling procedure. Blood samples were collected to determine HLA-C alleles by PCR at the Department of Microbiology & Immunology. Result was analyzed with SPSS software package version-26. ***Results:*** The controls were 36.8 ±14.2 years old, whereas the patients were 30.5± 15.8 years old on average. Plaque psoriasis was most prevalent, occurring among 75% of the case. Psoriasis patients had BMIs that were considerably higher than those of the controls. The most prevalent alleles were HLA-C*06 (47.5%) and HLA-C*07 (57.5%) in psoriasis patients and HLA-C*8 (40%) in controls. Female patients had a substantially greater frequency of HLA-C*06. There was no correlation found between HLA-C*06 and the patient's BMI,age of onset, psoriasis severity or pattern of psoriasis. ***Conclusions:*** Bangladeshi patients have shown association between HLA-C*06 and psoriasis. Additionally, female predominance has been shown in HLA-C*06 carrying patients.

Keywords: Psoriasis, genetic background, HLA-C*06.

INTRODUCTION

Psoriasis is a multifactorial disorder with a global prevalence ranging from 0.9% to 11%, while in Bangladesh it is estimated to be 0.7% [1,2]. Genetic factors, immunological dysregulations, and environmental triggers contribute to its pathogenesis. Psoriasis has a strong hereditary component: if both parents are affected, up to 50% of their children may also develop the condition, whereas the risk is 16% if one parent is affected and 8% if only a sibling is affected [3]. Monozygotic twins have 2–3 times higher concordance than dizygotic twins [3]. Several susceptibility loci (PSORS1–PSORS9) have been identified, with the PSORS1 locus on chromosome 6p21 showing the strongest association, accounting for 35–50% of heritability [4,5].

HLA-C*06 within the PSORS1 locus has shown the closest association with psoriasis susceptibility. Its exact function remains unclear, though

it may influence both the innate and adaptive immune systems [6]. HLA-C*06 can interact with killer immunoglobulin-like receptors (KIR2DL1), affecting lymphocyte activity and antigen presentation to T cells. LL-37, an overexpressed antimicrobial peptide in psoriasis, is presented by HLA-C*06 to CD8+ T cells and dendritic cells, triggering cytokine release (e.g., IFN-γ, TNF-α, IL-12, IL-23) [7]. Another potential autoantigen, ADAMTSL5, also binds HLA-C06 and induces IL-17A production [7].

Globally, the frequency of HLA-C*06 varies from 14.1% to 59.1% in the general population and 10.5% to 77.2% in psoriasis patients [6]. HLA-C*06 influences disease course, phenotype, severity, comorbidities, and treatment response [6]. Among Caucasians, HLA-C*06 carriers are nearly 10 times more likely to develop psoriasis. Homozygous carriers have about 2.5 times greater disease risk than heterozygous carriers [4]. Early-onset psoriasis (Type 1) is associated with HLA-C*06, and C*06-positive women tend to present earlier than men [6]. The allele is also more common in guttate psoriasis and is associated with widespread plaques, Koebner's phenomenon, sunlight improvement, and less nail involvement [6].

In Han Chinese patients, obesity coupled with HLA-C*06 conferred a 35-fold higher risk of psoriasis compared to normal-weight non-carriers [8]. HLA-C*06 is linked with delayed development of psoriatic arthritis [9]. While Eder et al. reported that HLA-C*06 was associated with severe atherosclerosis [9], Queiro et al. found a favorable cardiometabolic profile in C*06 carriers [10]. Douroudis et al. also observed lower rates of diabetes and cardiovascular disease in C*06-positive individuals [11]. Pregnancy-related remission is more common in C*06-positive patients [11].

METHODS

The case control study took place at Dermatology and Venereology department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh over a period from July 2021 to June Following consecutive sampling procedure, 40 psoriasis patients (diagnosed based on history, clinical feature and/or histopathological report) were enrolled who had no features of psoriatic arthritis. Similarly,40 apparently healthy controls who had no psoriasis, psoriatic arthritis or family history of psoriasis were included as control. Informed written consent was acquired from every participant or their legal guardian if they were under 18 years. Height, weight as well as body mass index (BMI) of all respondents were assessed. Each patient's disease severity was evaluated using the Psoriasis Area & Severity Index (PASI) as a measuring tool. A PASI score≤ 10 was regarded as indicative of mild disease, while a score >10 was considered to be moderate to severe disease. Blood sample was collected from each patient & control for HLA typing by PCR. The analysis of data was performed with the utilization of the SPSS version 26.0 for Windows. The analysis of the association of HLA-C*06 with age, BMI and age of onset of psoriasis was conducted using an independent sample t test. Chi-Square (X2) or Fisher's exact test was done to assess the correlation of HLA-C*06 with psoriasis pattern and severity. Univariate logistic regression analysis was conducted for predicting any risk of specific HLA-C allele in onset of psoriasis. Results were summarized by using odds ratios as well as 95% confidence intervals and p values. A "p" value below 0.05 was regarded significant for all statistical analysis.

RESULTS

Table-I: Comparison of baseline characteristics between two groups (n=80)

Baseline characteristics		**Control**	**Case**	**p-value**
		(n=40)	(n=40)	
		No. (%)	No. (%)	
Age group (in years)				
	<30	13(32.5%)	21(52.5%)	
	31-40	11(27.5%)	10(25.0%)	
	41-50	9(22.5%)	5(12.5%)	
	>50	7(17.5%)	4(10.0%)	
	Total	40(100.0%)	40(100.0%)	
	Mean ± SD	36.8±14.2	30.5±15.8	
				0.065
	Range (min-max)	(9-62)	(3.5-65)	
Gender				
	Male	21(52.5%)	23(57.5%)	
				0.653
	Female	19(47.5%)	17(42.5%)	
	Male: Female ratio	1.1:1	1.4:1	

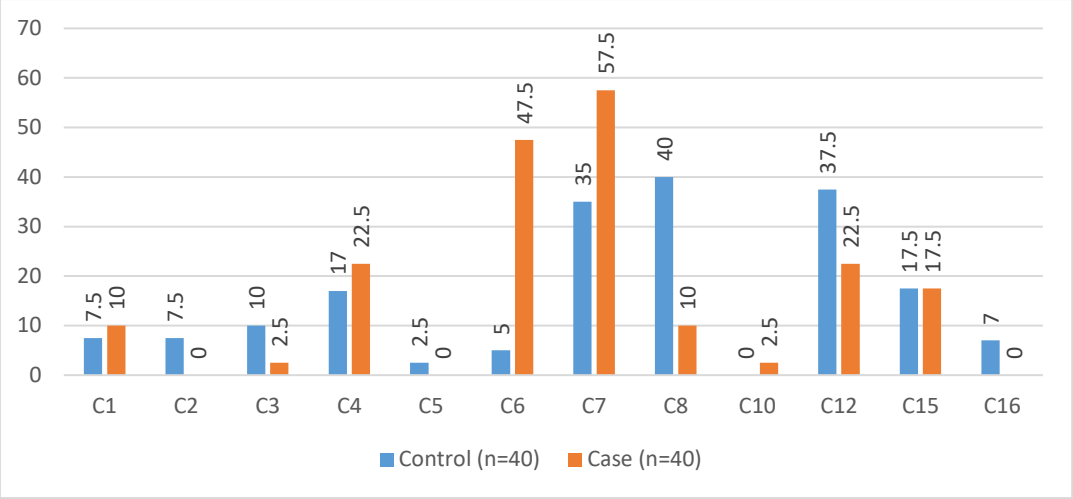

Figure I: Frequency of HLA-C alleles among cases and controls (n=80)

HLA-C alleles frequency were observed among 40 patients and 40 controls. It was found that more HLA-C*06 allele in psoriasis patients than healthy subjects (47.5% Vs 5.0 %) & the difference was significant. Also, a statistically significant higher frequency of HLA-C*07 was reported both in case (57.5%) and control (35%) . HLA-C*08 allele was found more frequently in healthy subjects (40.0%) than the psoriasis patients (10%); the difference of which was statistically significant.

Table- II: Association of age of onset of Psoriasis between HLA-C*06 subgroups (n=40)

HLA-C*06	N		Age of onset Psoriasis		p-value
		<40 years		≥ 40 years	
Positive	19	17(89.5%)		2(10.5%)	
					0.451
Negative	21	17(81.0%)		4(19.0%)	

In table-II, the comparing the psoriasis onset age in between HLA-C*06 subgroups (n=40) showed no significant difference.

Table-III: Association of gender of psoriatic patients between HLA-C*06 subgroups (n=40)

HLA-C*06 status	N		Gender		p-value
		Male		Female	
Positive	19	5(26.3%)		14(73.7%)	
					0.011
Negative	21	14(66.7%)		7(33.3%)	
Total	40	19(47.5%)		21(52.5%)	

Table-III shows among patients with HLA-C*06 positivity, 73.7% were female and only 26.3% were male. The association between HLA-C*06 positive patients and female gender was found to be statistically significant (p=0.011).

Table-IV: Association of disease severity of Psoriasis between HLA-C*06 subgroups (n=40)

HLA-C*06 status	N		Disease severity		p-value
		Mild (≤10)		Moderate to severe	
				>10)	
Positive	21	15(78.9%)		4(21.1%)	
					0.835
Negative	19	16(76.2%)		5(23.8%)	

This table shows no association of disease severity with HLA-C*06 status (p = 0.835).

Table-V: Association of types of psoriasis between HLA C*06 subgroups (n=40)

Type of psoriasis		HLA-C*06 status		p-value
	Positive		Negative	
	(n=19)		(n=21)	
Psoriasis vulgaris	15(78.9%)		15(71.4%)	
Palmoplantar psoriasis	2(10.5%)		3(14.3%)	0.486
Guttate psoriasis	2(10.5%)		1(4.8%)	
Erythrodermic psoriasis	0(0.0%)		2(9.5%)	
Total	19(100.0%)		21(100.0%)	

Table-V shows maximum HLA-C*06 positive patients suffered from psoriasis vulgaris while others from palmoplantar psoriasis (10.5%), Guttate psoriasis (10.5%) and erythrodermic psoriasis (10.5%). No association that was statistically significant was found between psoriasis types and HLA-C*06 subgroups.

Discussion

Over the last decade, advances in genetics have led to the discovery of several psoriasis-associated alleles. Our study evaluated the frequency of HLA-C alleles and the association of HLA-C*06 with clinical characteristics of psoriasis.

We found no significant age or gender differences between cases and controls, indicating minimal confounding effects. HLA-C*06-positive individuals had a 17.19 times higher risk, and HLA-C*07-positive individuals a 2.51 times higher risk of developing psoriasis, consistent with previous studies. Shankarkumar reported ORs of 17.7 and 6.5 for HLA-C06 and HLA-C02, respectively [16]. Indhumathi et al. observed an OR of 3.5 for HLA-C06 [13], while Anandan et al. reported ORs of 9.75 (HLA-C06) and 2.06 (HLA-C07) [17]. These findings highlight the pathogenic role of HLA-C*06 in psoriasis.

In our study, 73.7% of HLA-C06-positive patients were female, a statistically significant difference. This aligns with Indhumathi et al. who reported a female predominance among HLA-C06 carriers ($p = 0.006$; OR = 2.49) [13], and Douroudis et al., who also noted higher frequency in females [11]. However, a study by Łuszczek et al. found no gender difference [18]. The sex-based disparity may be attributed to factors such as microRNA expression from the X chromosome, differential T-regulatory cell levels, and hormonal effects like reduced postmenopausal estrogen levels, which dampen T-cell responsiveness [6].

In our study, 78.9% of HLA-C*06-positive patients had mild psoriasis, and 21.1% had moderate to severe disease, although this association was not statistically significant. Indhumathi et al. similarly found no relationship between HLA-C*06 and severity [13]. In contrast, Kim et al. and Queiro et al. reported that C*06-positive patients had higher PASI scores and more severe disease [19,10]. One explanation for the discrepancy is that our sample included treated patients and a proportion with palmoplantar involvement, potentially reducing the average PASI score. Larger studies may better establish this relationship.

Though not statistically significant, plaque psoriasis (78.9%) and guttate psoriasis (10.5%) were more common in HLA-C*06-positive individuals. This trend is in line with earlier studies by Gudjonsson et al. [12] and Douroudis et al. [11], who reported a higher frequency of guttate psoriasis among C*06-positive patients.

Conclusions

Psoriasis patients have a significant association with HLA-C*06 in Bangladesh. Moreover, female psoriatic patients are associated predominantly with HLA-C*06

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