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Original Article

Dermatology Section

Association of Human Leukocyte Antigen-Cw6 in Psoriasis Patients with Disease Severity and Morphological Patterns: A Cross-control Study in a Tertiary Care Referral Centre in Eastern India

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ABSTRACT

Introduction: Psoriasis is a multifactorial disorder in which genetic and environmental factors play an essential role in disease pathogenesis. The Human Leukocyte Antigen-Cw6 (HLA-Cw6) allele has shown the strongest genetic association with this condition across several populations studied.

Aim: To estimate the risk of HLA-Cw6 association with psoriasis compared to the control group and its association with the severity of psoriasis expressed as Psoriasis Area and Severity Index (PASI) score and morphological patterns.

Materials and Methods: A cross-control study was conducted from March 2014 to February 2015 in a tertiary care centre in the eastern part of India. All patients who were diagnosed clinically as psoriasis and gave written informed consent were included in the study. Healthy controls were taken to compare the HLA-Cw6 after duly signing the informed consent for detailed history, clinical examination, PASI score, and digital photographs of lesions were taken. A blood sample was taken from patients and the control for HLA-Cw6 typing by sequence-specific Polymerase Chain Reaction (PCR) method. Data was analysed by appropriate statistical test (Chi-square test) using R statistical software.

Results: A total of 100 patients with psoriasis and 100 controls were recruited, of which 61 were positive for HLA-Cw6 among the psoriasis group and nine in the control group. Positivity of the HLA-Cw6 allele was significantly higher in psoriasis cases (n=61) compared to normal individuals (n=9) (p-value: 1.79×10^{-15}, OR: 15.8148, 95% CI: 7.15-34.99). It was also observed that HLA-Cw6 positive individuals had a more severe form of the disease, determined by a PASI score >6 (p-value: 0.0494, OR: 2.22, 95% CI: 0.96-5.15), and significant involvement of scalp psoriasis (p-value: 0.0054, OR: 13.125, 95% CI: 1.55-111.42). However, no significant association of HLA-Cw6 was seen with positive family history, nail involvement, and joint pain (arthralgia).

Conclusion: The HLA-Cw6 positivity was associated with a more severe form of disease and scalp psoriasis.

Keywords: Morphological patterns, Nail involvement, Polymerase chain reaction, Psoriasis area and severity index

INTRODUCTION

Psoriasis is a common, chronic, recurrent skin disease that is immune-mediated with a strong genetic component, but environmental factors like infections also play an important role in the presentation of the disease [1]. Its prevalence varies from 0.44-2.8% in India. The disease has an unpredictable course and complex aetiology. Morphologically the disease presents with different clinical patterns, the commonest being plaque type. The other variants are guttate, inverse or flexural, nail psoriasis, scalp psoriasis, psoriatic arthritis, pustular and erythrodermic [2]. Nail involvement in psoriasis can occur in 10-78% of patients [3]. PASI score is used to calculate the extent of involvement and severity of psoriasis [4]. Many psoriasis susceptibility loci have been identified on genome-based scans. Genome-wide linkage analyses have shown an association of psoriasis with a locus on chromosome 6p in which HLA-Cw6 is more likely susceptible allele in the Psoriasis Susceptibility Locus 1 (PSORS1), seen up to 50% of disease inheritability [5,6]. In a recent study, on the Indian Tamil ethnic population, HLA-Cw6 is strongly associated with psoriasis [7]. Further, in Eastern India, no studies have been done on HLA-Cw6 and psoriasis regarding the disease severity and morphological pattern. Thus, the study aimed to estimate the risk of HLA-Cw6 association with psoriasis compared to the control group and to explore the association between HLA-Cw6 haplotype with the severity of psoriasis expressed as PASI score and morphological patterns.

MATERIALS AND METHODS

A cross-control study was conducted from March 2014 to February 2015 at Department of Dermatology, Institute of Post-Graduate Medical Education and Research, Kolkata (West Bengal), a tertiary care centre in the eastern part of India. Total 100 patients were taken into study and those patients coming to OPD not having psoriasis were taken as control. This study was approved by Institutional Ethics Committee (IEC No. 441).

Inclusion criteria: All consecutive patients coming to Department of Dermatology Outpatient Department (OPD) and first time diagnosed clinically with psoriasis and willing to give written informed consent were included in the study.

Exclusion criteria: Patients not giving informed written consent, exclusive palmoplantar psoriasis, and psoriasis patients associated with other autoimmune diseases were excluded from the study.

Study Procedure

Detailed history, clinical examination, and PASI score and digital photographs of lesions were taken [8]. Skin biopsy was taken to confirm the diagnosis in doubtful cases. A blood sample was taken from each patient for HLA-Cw6 typing by sequence-specific PCR method.

STATISTICAL ANALYSIS

Data analysis was done by appropriate statistical test (Chi-square test) (p-value <0.05) using R statistical software.

RESULTS

A total of 100 patients with psoriasis were recruited, of which 39 were female, and 61 were male. The minimum age of the patient was 8 years, and the maximum was 81 years and mean age (years) was 35.12±15.5. Out of 100 psoriasis patients, 61 were positive for HLA-Cw6, while amongst 100 control subjects, only nine were HLA-Cw6 positive. HLA-Cw6 distributions and association in psoriasis patients and control group is depicted in [Table/Fig-1].

Groups	Cw6+	Cw6-	Odds ratio	95% CI	p-value
Cases	61	39	15.8148	7.1484-34.9882	1.79E-15*
Controls	9	91			

[Table/Fig-1]: HLA Cw6 distributions and association in total cases (n=100) vs. total controls (N=100).
*significant p-value

HLA-Cw6 positive psoriasis patients had significantly associated with severe disease (PASI >6) compared to mild disease (PASI ≤6). Association of HLA-Cw6 according to PASI score is depicted in [Table/Fig-2].

PASI score	Cw6+ (n=61)	Cw6-(n=39)	Odds ratio	95% CI	p-value
Mild (<6)	17	18	2.22	0.96-5.15	0.0494*
Moderate to severe (>6)	44	21			

[Table/Fig-2]: HLA Cw6 distributions and association according to disease severity.
*significant p-value

A significant proportion of HLA -Cw6 positive patients had scalp involvement compared to HLA-Cw6 negative patients. However, there were no significant difference in nail involvement, arthralgia, and family history with HLA-Cw6 positive patients as compared to HLA-Cw6 negative patients. HLA-Cw6 distribution and association according to clinical involvement is depicted in [Table/Fig-3].

Clinical involvements	Cw6+ (n=61)	Cw6- (n=39)	Odds ratio	95% CI	p-value
Nail involvement	21	14	2.4	0.9066-6.3537	0.523757196
Family history	12	5	1.6653	0.5372-5.1619	0.272105968
Scalp involvement	60	32	13.125	1.5461-111.4216	0.00537252*
Arthralgia	10	4	1.8617	0.5391-6.4293	0.245108566

[Table/Fig-3]: HLA Cw6 distributions and association according to clinical involvements.
*significant p-value

There were no significant associations in clinical types of psoriasis with HLA-Cw6 positive patients compared to negative patients. HLA-Cw6 distribution and association according to morphological patterns is depicted in [Table/Fig-4].

Clinical types	No. of patients	HLACw6+ (n=61)	HLA Cw6- (n=39)	p-value
Generalised plaque	93	58	35	0.264140
Guttate	4	3	1	0.491036
Erythrodermic	2	0	2	
Pustular	1	0	1	

[Table/Fig-4]: HLA Cw6 distributions and association according to morphological patterns.

DISCUSSION

The present study included 100 patients with psoriasis attending the dermatology OPD of a tertiary care centre in the eastern part of India. It was found that a statistically significant proportion of psoriasis patients were HLA-Cw6 positive than the control group (p-value: 1.79×10^{-15}). A study done by Singh S et al., amongst north Indian patients (sample size=75) with psoriasis showed a significant association with HLA-Cw6 positivity [9]. Apart from this, other studies done by Kastelan M et al., in Croatian population (sample size=108) and Kim TG et al., in Korean population (sample size=84) also had similar findings [10,11]. This finding supports a strong association of psoriasis with HLA-Cw6 positivity in different geographical regions.

A HLA-Cw6 positive psoriasis patients showed higher PASI scores. It was found that PASI score >6 (moderate to severe) had a significant association (p-value: 0.0494) with HLA-Cw6 but not with mild disease. This study was similar to a study done by Sathishkumar D et al., in southern Indian children (sample size=108), in which a higher PASI score (>10) was significantly associated with HLA-Cw6 positivity [12]. Another study among South Indian ethnic population (sample size=100) showed moderate PASI score (5-10) associated with HLA-Cw6 positivity. Similar study done by Fan X et al., among Han Chinese population in a cohort of 679 patients showed HLA-Cw6 positive patients had severe disease (PASI score >15) [13].

It was found that there were no significant differences in nail involvement with HLA-Cw6 positive patients as compared to HLA-Cw6 negative patients (p-value: 0.523757196). In a study done by Gudjónsson JE, in 369 patients with familial psoriasis, 138 patients had psoriatic nail changes but no significant association with HLA-cw6 was found. A study done by Indhumathi S et al., in 355 southern Indian Tamil psoriasis patients, 122 patients had nail involvement (p value-0.11) [14,15].

A total of 17 patients (N=100) had a positive family history, in which 12 were positive for HLA-Cw6. It was found that there was no significant differences (p-value: 0.272105968) in family history with HLA-Cw6 positive patients as compared to HLA-Cw6 negative patients. Similarly in study done by Bahcetepe N et al., also found no significant differences in family history [16]. However, another study by Ilkäheimo I et al., in Omani Arab population shown HLA-Cw6 had a stronger correlation with an overall positive family history [17]. This may be due to difference in geographical regions.

There was a statistically significant association seen in HLA-Cw6 positive patients with scalp involvement in comparison to HLA-Cw6 negative patients (p-value: 0.00537252). A study done in southern Indian population on childhood psoriasis by Sathishkumar D et al., showed HLA-Cw6 was associated with scalp involvement [12]. There are very few studies done in Indian population to show relationship between scalp involvement in psoriasis and HLA-Cw6. These studies confirm that HLA-cw6 may link to pathogenesis of scalp psoriasis.

Ten out of 14 patients with arthralgia were positive for HLA-Cw6, suggesting no significant difference (p-value: 0.245108566) than HLA-Cw6 negative patients. A study done by Fan X et al., among Han Chinese population showed no significant difference in arthralgia with HLA-Cw6 positive patients as compared to HLA-Cw6 negative patients (p-value-0.733) [13].

Among all patients (N=100), the most common morphological type was plaque type (93), followed by guttate, erythrodermic, and pustular types. It was found that there was no significant association of HLA-Cw6 positive patients with these morphological types. Similar study results were shown by Fan X et al., and Indhumathi S et al., for generalised plaque type of psoriasis and erythrodermic psoriasis. However, in their studies, gutted type of psoriasis had a significant association with HLA-Cw6 [13,15]. This difference found in the study may be due to large sample size taken by those authors due to which study variables have increased and more clinical varieties of psoriasis were seen.

Limitation(s)

Because of the low prevalence of psoriasis, study subject was limited to 100. Demographic characteristic of the control group was not included in the study.

CONCLUSION(S)

This study amongst 100 patients having psoriasis observed a significant association of HLA-Cw6 with the severity of disease and involvement of specific sites like the scalp. However, further study with a larger population may further improve our knowledge of psoriasis, its genetic basis, and various manifestations.

REFERENCES

[1] Langley RG, Krueger GG, Griffiths CE. Psoriasis: Epidemiology, clinical features, and quality of life. Ann Rheum Dis. 2005;64:18-23.
[2] Dogra S, Yadav S. Psoriasis in India: Prevalence and pattern. Indian J Dermatol Venereol Leprol. 2010;76:595.
[3] Dogra A, Arora AK. Nail psoriasis: The journey so far. Indian J Dermatol. 2014;59:319.
[4] Peter CM, Kerkhof VD, Nestle FO. Psoriasis. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology, 4th ed. Elsevier; 2018. Pp. 138-60.
[5] Nair RP, Stuart PE, Nistor I, Hiremagalore R, Chia NV, Jenisch S, et al. Sequence and haplotype analysis supports HLA-C as the psoriasis susceptibility 1 gene. Am J Hum Genet. 2006;78:827-51.
[6] Trembath RC, Lee Clough R, Rosbotham JL, Jones AB, Camp RD, Frodsham A, et al. Identification of a major susceptibility locus on chromosome 6p and evidence for further disease loci revealed by a two stage genome-wide search in psoriasis. Hum Mol Genet. 1997;6:813-20.
[7] Anandan A, Thokala R, Radhakrishnan K, Panicker VK, Sundaram M. Association of HLA-C*06 with psoriasis in a tertiary care hospital. J Evolution Med Dent Sci. 2020;9:1563-66.
[8] Fredriksson T, Pettersson U. Severe psoriasis-oral therapy with a new retinoids. Dermatology. 1978;157:238-44.
[9] Singh S, Singh U, Singh S. Human leukocyte antigen in patients with psoriasis. Indian J Dermatol Venereol Leprol. 2011;77:535.
[10] Kastelan M, Gruber F, Cecuk E, Kerhin-Brkljacić V, Brkljacić-Surkalović L, Kastelan A. Analysis of HLA antigens in Croatian patients with psoriasis. Acta Derm Venereol Suppl. 2000;2:80.
[11] Kim TG, Han H, Lee HJ, Youn JI, Kim TY. The association of psoriasis with human leukocyte antigens in Korean population and the influence of age of onset and sex. J Invest Dermatol. 2000;114:309-13.
[12] Sathishkumar D, George R, Daniel D, Peter JV. Clinical profile of childhood-onset psoriasis and prevalence of HLA-Cw6: A hospital-based study from India. Postgrad Med J. 2015;91:309-14.
[13] Fan X, Yang S, Sun LD, Liang YH, Gao M, Zhang KY, et al. Comparison of clinical features of HLA-Cw* 0602-positive and-negative psoriasis patients in a Han Chinese population. Acta Derm Venereol. 2007;87:47-52.
[14] Gudjónsson JE. HLA-Cw6-positive and HLA-Cw6-negative patients with Psoriasis vulgaris have distinct clinical features. J Invest Dermatol. 2002;118:362-65.
[15] Indhumathi S, Rajappa M, Chandrashekar L, Ananthanarayanan PH, Thappa DM, Negi VS. The HLA-C*06 allele as a possible genetic predisposing factor to psoriasis in South Indian Tamils. Arch Dermatol Res. 2016;308:193-99.
[16] Bahcetepe N, Kutlubay Z, Yilmaz E, Tuzun Y, Eren B. The role of HLA antigens in the aetiology of psoriasis. Med Glas (Zenica). 2013;10:339-42.
[17] Ikäheimo I, Tiilikainen A, Karvonen J, Silvennoinen-Kassinen S. HLA risk haplotype Cw6,DR7,DQA1*0201 and HLA-Cw6 with reference to the clinical picture of psoriasis vulgaris. Arch Dermatol Res. 1996;288:363-65.

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