HLA-B and HLA-C Locus Alleles in Psoriasis: Study in a Tertiary Care Hospital of Bangladesh

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Submission Date : 02 April 2024
Accepted Date : 07 August 2024
Published Date : 30 September 2024
DOI: https://doi.org/10.3329/jrpmc.v9i2.77294

Abstract:

Background:
Psoriasis is a common autoimmune disorder with regional and ethnic differences in its prevalence and clinical manifestations. It is known to be associated with the presence of certain specific Human Leukocyte Antigen (HLA) alleles and characterized by T cell-mediated keratinocyte hyperproliferation. Genetic factors are also important in both susceptibility to and the expression of psoriatic arthritis. A significant portion of psoriatic arthritis patients develop psoriasis after arthritis manifestation. So, it may be helpful if we could identify the HLA alleles involved in patients with psoriasis and in patients with psoriatic arthritis. Through the HLA alleles pattern, we can identify those psoriatic arthritis patients earlier who develop arthritis manifestations without psoriasis and treat them appropriately.

Objective:
To detect HLA-B and HLA-C alleles that may contribute to the genetic susceptibility to psoriasis in Bangladeshi patients.

Methods:
This cross-sectional study was carried out on patients with psoriasis in outpatient department of Rheumatology, outpatient department of Dermatology, department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University from March 2015 to April 2017 on 33 patients diagnosed as psoriasis clinically by both rheumatologist and dermatologist compared with 30 controls having no history or family history of psoriasis.

Results:
In this study we found that there are increased frequencies of HLA-B*57 (39.4%, OR-1.4, *P*=0.52), B*35 (21.2%, OR-1.04, *P*=0.9), B*44 (18.2%, OR-1.05, *P*=0.87) and C*6 (18.2, OR-1.05, *P*=0.87) in psoriatic patients. These alleles were also identified in increased frequency in control subjects.

Conclusion:
HLA-B*44, B*57, B*35 and C*6 and C*7 alleles were detected in increased frequency in psoriatic patients although these were also frequent in normal subjects. It needs a further study which includes a large sample size to find out association with psoriasis.

Keywords: Psoriasis, HLA alleles

Citation: Islam MT,Akhtar R,Ahmed S,Asaduzzaman ATM, Karim MN, Sarkar MRA,Anwar MMU, Islam MA,Choudhury MMR, Haq SA.HLA-B and HLA-C Locus Alleles in Psoriasis: Study in a Tertiary Care Hospital of Bangladesh.J Rang Med Col. 2024 Sep;9(2):3-7.doi:https://doi.org/10.3329/jrpmc.v9i2.77294

Introduction:

Psoriasis is a chronic inflammatory skin disease where T-cell mediated hyperproliferation of keratinocytes is the characteristic feature. Environmental and genetic factors both are associated with psoriasis as etiological factors.[1] Worldwide distribution of psoriasis varies among ethnic groups and geographical locations, peak prevalence of which is about 2% of the world population. Psoriasis associated with strong but complex genetic background. Concordance rate is approximately 60% in monozygotic twins.[2] A

Genome Wide Association Study (GWAS) revealed that there is highest degree of differential association between HLA-C and HLA-B in the major histocompatibility complex (MHC) class I.[3] According to results of population studies HLA-C*06 is associated with early-onset psoriasis that is more likely to be familial.[4] Several population and family studies also reported that psoriasis is significantly associated with HLA-HLA-A*01, A*02, B13, B17, B39, B57, Cw*06, Cw*07, and DR7, DQA1*0201.[5-12] In psoriasis, susceptibility of the HLA-C locus on chromosome 6p21.33 is acceptable as reported by several genetic studies. The association between psoriasis and the HLA-C*06 allele has been demonstrated.[13-16]

In Bangladesh the reports regarding association of HLA alleles and psoriasis are lacking. So, we aimed to investigate the association of HLA-B and HLA-C alleles and psoriasis in Bangladeshi population though the study population size is very small.

Methods:

This cross-sectional pilot study was carried out on patients with psoriasisin outpatient department of Rheumatology, outpatient department of Dermatology, department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University from March 2015 to April 2017.Patients with psoriasis (n=33) attending the outpatient department of Rheumatology, and outpatient department of Dermatology for their treatment, constituted the study population. Postgraduate medical students, nursing staff and employees working in the outpatient department of BSM Medical University having no history of psoriasis and also had no family history of psoriasis were enrolled as control (n=30).Convenient sampling was done as a sampling procedure.HLA tissue typing was performed by using The Morgan™ HLA SSP ABDR typing Kit. All the data was checked and edited after collection. Then the data were entered into the computer, processed and analyzed using the computer-based software SPSS (Statistical Package for Social Sciences) version 17. The Statistical terms included in this study are mean, standard deviation, percentage. HLA antigens were correlated with all variables mentioned by chi-square test.

Results:

We have enrolled thirty-three (33) patients with psoriasis and thirty (30) normal control subjects in this study. In psoriatic patients mean age was 37.07± 10.84 years compared with 31.07±7.66 years in control. Male and service holder was predominant in both groups.(Table-I).

Table-I: Demographic characteristics of the study patients and controls (N=63)

Demographic characteristics	Control (n=30) no.(%)	Psoriasis (n=33) no.(%)
Age in Year (Mean ± SD)	31.07±7.66	37.48±10.84
Sex		
Male	19(63.3)	23(69.7)
Female	11(36.7)	10(30.3)
Occupational Status		
Housewife	2(6.7)	6(18.2)
Laborer	0(0.0)	8(24.2)
Garment worker	1(3.3)	0(0.0)
Student	0(0.0)	3(9.1)
Service holder	27(90.0)	15(45.5)
Teacher	0(0.0)	1(3.0)
Other	0(0.0)	0(0.0)
Marital Status		
Married	25(83.3)	29(87.9)
Unmarried	5(16.7)	4(12.1)
Residence Status		
Urban	23(76.7)	7(21.2)
Rural	7(23.3)	26(78.8)

The duration of psoriasis was 65.91±61.11 months and age of onset of psoriasis was 32.39± 10.28years. In Six (18%) patients only scalp was involved and in two (6.1%) patients only knee was involved but in 25(75.8%) patients multiple sites of the body were affected (Table-II).

Table-II: Clinical characteristics of Psoriasis (N=33)

Clinical features	no.(%)
Duration in Months (Mean ± SD)	65.91 ± 61.11
Age of onset in Years (Mean ± SD)	32.39 ± 10.28
Sites of Psoriasis	
Scalp	6(18.2)
Back of elbow	0(0.0)
Nail	0(0.0)
Knee	2(6.1)
Sacral region	0(0.0)
Others	25(75.8)

HLA-B*57 was present in 13(39.4%) patients with psoriasis and in 7(23.3%) among the control subjects (OR=1.40, p=0.52). HLA-C*4 was present

in 9(27.3%) (OR = 1.20, p=0.49), and HLA-C*6 was present in 6(18.2%) patients with psoriasis (OR = 1.05, p = 0.87) but HLA C*4 was present in 6(20%) and HLA-C*6 was present in 5(16.7%) in control subjects. HLA-C*5 was present in 3(10.0%) and HLA-C*3 was present in 3(10.0%) control subjects. HLA-C*5 was present in 1(3%) and HLA-C*3 in 1(3%) patient with psoriasis. HLA-C*7 was present in increased frequency both psoriatic patients (48.5%) and control subjects (40%) (Table-III & Table-IV).

Table-III: Distribution of HLA-B alleles in patients and controls (N=63)

HLA-B alleles	Control (n=30) no. (%)	Psoriasis (n=33) no. (%)	OR	p-value
HLA-B7	1(3.3)	3(9.1)	1.48	0.22
HLA-B13	1(3.3)	3(9.1)	1.48	0.22
HLA-B15	7(23.3)	5(15.2)	0.76	0.45
HLA-B17	1(3.3)	0(0.0)	-	-
HLA-B27	5(16.7)	1(3.0)	0.30	0.19
HLA-B35	6(20.0)	7(21.2)	1.04	0.90
HLA-B37	3(10.0)	4(12.1)	1.10	0.78
HLA-B38	5(16.7)	2(6.1)	0.52	0.28
HLA-B39	0(0.0)	1(3.0)	1.94	<0.001
HLA-B44	5(16.7)	6(18.2)	1.05	0.87
HLA-B51	0(0.0)	1(3.0)	1.94	<0.001
HLA-B57	7(23.3)	13(39.4)	1.40	0.52

*chi-square test

Table-IV: Distribution of HLA-C alleles in Patients and Controls (N=63)

HLA- C alleles	Control (n=30) no. (%)	Psoriasis (n=33) no. (%)	OR	p-value
C1	4(13.3)	0(0.0)	-	-
C2	3(10.0)	0(0.0)	-	-
C3	3(10.0)	3(9.1)	0.46	0.38
C4	6(20.0)	9(27.3)	1.20	0.48
C5	3(10.0)	3(9.1)	0.46	0.38
C6	5(16.7)	6(18.2)	1.05	0.87
C7	12(40.0)	16(48.5)	0.18	0.50
C8	3(10.0)	3(9.1)	0.95	0.90
C9	0(0.0)	0(0.0)	-	-
C10	2(6.7)	2(6.1)	0.95	0.92

*chi-square test

Discussion:

Shankar Kumar Umapathyet al[17] showed that HLA-A*2, B*8 and B*17 have a strong association with psoriasis that also indicates their susceptibility but HLA-A*28, B*5 and B*12 have a strong negative association. They also reported that HLA-B*13, B*17, B*37, B*39 and Cw*6 have a good correlation with psoriasis and HLA-B*38, B*39, B*27, B*17 and Cw*6 have association with psoriatic arthritis. Goodjonsson JE[4] et al reported that the linkage and high-resolution association studies strongly indicate that HAL-Cw*0602 had a major susceptibility risk in psoriasis. In our study HLA-B*13, B*35, B*37, B*44, B*57and C*4, C*6 and C*7 were more frequent psoriatic patients than the control subjects although it was insignificant. HLA-B*57 was detected in increased frequency in patients with psoriasis as reported by some studies from Chinese[18] and found in increased in type I psoriasis in Germany[19] and Thailand[20-21]. In our study HLA-B*57 was also more frequent in psoriatic patients than the controls. ApiwatSangphukieo et al[22] first reported that in type I psoriasis HLA-B*13:01 may be associated with pustular psoriasis. In our study HLA-B*13 was found in increased frequency in study patients. Sangeeta Sngh et al[23] reported that HLA-B*17 was detected in patients with psoriasis in their patients though it was insignificant. HLA-B*17 was also revealed in increased frequency in patients with psoriasis in this study. HLA-Cw*6 was also detected in psoriatic patients more frequently than the control subjects as reported by Sangeeta Singh et al.[24] CassiaFF et al[24] also reported increased frequency of HLA-Cw06 in psoriatic patients in comparison to controls. In our study we also found that HLA-C*6 was more frequent in psoriatic patients than the controls. In one study it was found that HLA-C*07 allele was significantly associated with late age of onset suggesting it could be biomarker of late onset of psoriasis in Moroccan patients.[25] Only a few studies reported that there is an association between HLA-C*7and psoriasis. HLA-C*7 was also more frequent in study patients in this study.

Conclusion:

In this pilot study HLA-B*57, HLA-B*44, HLA-C*6 and HLA-C7 were more frequent in patients with psoriasis than the normal control subjects although it was not significant. It needs further research with large cohort to see the association of HLA alleles with psoriasis, type and onset of psoriasis and their association with psoriatic arthritis.

Limitations:

The small sample size is a notable limitation of this

study.

Acknowledgement:
Authors would like to thank Md. Sharif Hassan, Senior Statistician, International Center for Diarrheal Disease Research Bangladesh (ICDDR, B) for statistical analysis.

Funding: This work was supported by Asia Pacific League of Associations for Rheumatology (APLAR).

Ethical approval: Ethical committee of BSM Medical University, Dhaka, Bangladesh.

Conflicts of Interest: Nothing to disclose

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