HLA class II alleles and haplotypes in multiple sclerosis patients from eastern Saudi Arabia

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INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease with a strong genetic component involving the HLA class II region. However, HLA associations may vary among populations. This study investigated HLA-DRB1 and HLA-DQB1 allele and haplotype distributions in MS patients from Eastern Saudi Arabia and evaluated their associations with disease susceptibility.

OBJECTIVE

To identify HLA-DRB1, HLA-DQB1, and DRB1~DQB1 haplotypes associated with MS susceptibility in an Eastern Saudi Arabian population.

METHODS

Retrospective analysis of MS patients who were diagnosed according to the revised McDonald criteria at King Fahad Specialist Hospital-Dammam.

117
MS patients
HLA-DRB1 & HLA-DQB1 genotyping

1,582
Healthy controls
HLA-DRB1 & HLA-DQB1 genotyping

Allele and haplotype frequency analysis
HLA-DRB1, HLA-DQB1 and DRB1~DQB1 haplotypes

Association testing
OR + 95% CI + p-value

HOW TO READ THE RESULTS

- **Increased susceptibility** · OR > 1, p < 0.05
- **Reduced susceptibility** · OR < 1, p < 0.05
- **Not significant** · p ≥ 0.05
- **No association** · OR = 1 (log-scale axis)
- **Square = odds ratio** · line = 95% CI

RESULTS · DRB1 ALLELES

DRB1*15 and **DRB1*04** were significantly associated with **increased susceptibility** to MS.

Allele	MS (freq)	Control (freq)	OR (95% CI)	p value
DRB1*15	0.19	0.11	**2.00** (1.40–2.87)	**0.0001**
DRB1*04	0.23	0.16	**1.49** (1.07–2.09)	**0.0187**
DRB1*08	0.02	0.02	1.22 (0.44–3.42)	0.7015
DRB1*12	0.01	0.01	1.09 (0.34–3.56)	0.8822
DRB1*10	0.08	0.08	0.94 (0.56–1.59)	0.8150
DRB1*03(18)	0.02	0.02	0.79 (0.29–2.19)	0.6520
DRB1*07	0.12	0.13	0.93 (0.60–1.43)	0.7375
DRB1*14	0.00	0.01	0.32 (0.04–2.34)	0.2374
DRB1*01	0.02	0.03	0.61 (0.22–1.67)	0.3293
DRB1*16	0.04	0.06	0.63 (0.31–1.30)	0.2080
DRB1*03(17)	0.13	0.15	0.81 (0.53–1.22)	0.3081
DRB1*11	0.08	0.10	0.70 (0.42–1.18)	0.1803
DRB1*13	0.07	0.10	0.65 (0.38–1.12)	0.1185

Odds ratio (log scale · 95% CI): 0.1 · 0.3 · 1 · 3 · 10
← Reduced susceptibility Increased susceptibility →

RESULTS · DQB1 ALLELES

DQB1*03(8) and **DQB1*03(9)** were significantly associated with **increased susceptibility** to MS.
DQB1*02 was significantly associated with **reduced susceptibility** to MS.

Allele	MS (freq)	Control (freq)	OR (95% CI)	p value
DQB1*03(9)	0.03	0.01	**2.8** (1.18–6.90)	**0.0151**
DQB1*03(8)	0.17	0.12	**1.41** (1.03–2.16)	**0.0321**
DQB1*04	0.05	0.03	1.41 (0.74–2.77)	0.2902
DQB1*06	0.24	0.2	1.18 (0.88–1.71)	0.2179
DQB1*03(7)	0.1	0.12	0.85 (0.52–1.32)	0.4385
DQB1*05	0.18	0.21	0.85 (0.57–1.17)	0.2647
DQB1*02	0.24	0.3	**0.78** (0.51–0.98)	**0.0375**

Odds ratio (log scale · 95% CI): 0.1 · 0.3 · 1 · 3 · 10
← Reduced susceptibility Increased susceptibility →

KEY FINDINGS

OR 6.16
DRB1*07~DQB1*03(9)
Strongest risk haplotype
p < 0.0001

OR 2.00
DRB1*15
Most significant allele
p = 0.0001

OR 1.9
DRB1*15~DQB1*06
Classical MS risk haplotype
p = 0.0007

OR 0.47
DRB1*13~DQB1*06
Protective haplotype
p = 0.0182

RESULTS · HAPLOTYPES

DRB1*15~DQB1*06, **DRB1*04~DQB1*03(8)**, **DRB1*07~DQB1*03(9)**, and **DRB1*13~DQB1*03(7)** were significantly associated with **increased susceptibility** to MS.
DRB1*13~DQB1*06 was significantly associated with **reduced susceptibility** to MS.

Haplotype	MS (freq)	Control (freq)	OR (95% CI)	p value
DRB1*15~DQB1*06	0.17	0.1	**1.9** (1.30–2.77)	**0.0007**
DRB1*04~DQB1*03(8)	0.17	0.12	**1.53** (1.05–2.21)	**0.0243**
DRB1*03(17)~DQB1*02	0.13	0.15	0.84 (0.55–1.27)	0.406
DRB1*07~DQB1*02	0.1	0.12	0.82 (0.52–1.30)	0.4011
DRB1*10~DQB1*05	0.08	0.08	0.94 (0.56–1.59)	0.8152
DRB1*11~DQB1*03(7)	0.05	0.09	0.57 (0.31–1.06)	0.074
DRB1*13~DQB1*06	0.05	0.1	**0.47** (0.25–0.89)	**0.0182**
DRB1*07~DQB1*03(9)	0.04	0.01	**6.16** (2.68–14.17)	**<0.0001**
DRB1*16~DQB1*05	0.03	0.06	0.49 (0.21–1.11)	0.0799
DRB1*13~DQB1*03(7)	0.02	0.01	**3.8** (1.41–10.22)	**0.0045**
DRB1*15~DQB1*05	0.02	0.01	**2.52** (0.97–6.57)	**0.0497**
DRB1*03(18)~DQB1*04	0.02	0.02	0.79 (0.29–2.19)	0.652
DRB1*04~DQB1*02	0.02	0.03	0.75 (0.30–1.86)	0.5297
DRB1*01~DQB1*05	0.02	0.03	0.61 (0.22–1.67)	0.3293
DRB1*11~DQB1*06	0.01	<0.01	3.01 (0.87–10.49)	0.0685
DRB1*03:01~DQB1*05	0.01	<0.01	2.73 (0.60–12.40)	0.1752
DRB1*04~DQB1*04	0.01	0.01	1.96 (0.58–6.58)	0.2672
DRB1*12~DQB1*05	0.01	0.01	1.58 (0.36–6.81)	0.5387
DRB1*11~DQB1*05	0.01	0.01	1.15 (0.27–4.88)	0.85
DRB1*08~DQB1*03(7)	0.01	0.01	0.85 (0.20–3.56)	0.8256
DRB1*16~DQB1*06	<0.01	<0.01	2.49 (0.30–20.82)	0.3821
DRB1*12~DQB1*03(7)	<0.01	0.01	0.68 (0.09–5.05)	0.7016
DRB1*14~DQB1*05	<0.01	0.01	0.33 (0.05–2.39)	0.2478

Odds ratio (log scale): 0.1 · 1 · 10
← reduced increased →

CONCLUSION

1. This study confirms the strong influence of HLA class II variation on MS susceptibility in the Eastern Saudi Arabian population, with both classical (**DRB1*15~DQB1*06**) and population-specific risk and protective haplotypes.
2. These findings highlight the value of regional HLA profiling in understanding MS pathogenesis in Arab populations.

SIGNIFICANT HAPLOTYPES

- Classical risk: DRB1*15~DQB1*06
- Additional risk: DRB1*04~DQB1*03(8), DRB1*07~DQB1*03(9), DRB1*13~DQB1*03(7)
- Protective: DRB1*13~DQB1*06