**Human leukocyte antigen complex and other immunogenetic and clinical factors influence susceptibility or protection to SARS-CoV-2 infection and severity of the disease course. The Sardinian experience.**

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**HLA alleles and haplotypes in patients and controls**

The HLA allele frequencies of a cohort of 619 Sardinian controls were compared to those observed in a group of 182 patients with SARS-CoV-2 infection.

The P values corrected for multiple comparisons between controls and patients (Pc) were obtained by multiplying the P values calculated according to the two-tailed Fisher’s exact test by the number of tested alleles (18 for HLA-A, 27 for HLA-B, 13 for HLA-C and 13 for HLA-DRB1).

The only alleles with Pc < 0.05 were:

HLA-B\*40 [Pc = 0.049, OR = 3.80 (1.52 – 9.59)]

HLA-C\*04 [Pc = 0.012, OR = 1.75 (1.25 – 2.43)].

Other alleles with P < 0.05, but with Pc higher than the significance threshold are highlighted in bold type in the following Tables.

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A****locus** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*11** | 81 | 6.54 | 36 | 9.89 | **0.0386** | 0.694 |
| A\*80 | 0 | 0 | 2 | 0.55 | 0.0515 | 0.927 |
| A\*66 | 1 | 0.08 | 2 | 0.55 | 0.131 | 1 |
| A\*26 | 28 | 2.26 | 14 | 3.85 | 0.133 | 1 |
| A\*30 | 230 | 18.58 | 56 | 15.38 | 0.186 | 1 |
| A\*03 | 65 | 5.25 | 26 | 7.14 | 0.197 | 1 |
| A\*25 | 2 | 0.16 | 2 | 0.55 | 0.224 | 1 |
| A\*33 | 45 | 3.63 | 8 | 2.20 | 0.242 | 1 |
| A\*29 | 26 | 2.10 | 4 | 1.10 | 0.274 | 1 |
| A\*32 | 108 | 8.72 | 38 | 10.44 | 0.351 | 1 |
| A\*01 | 102 | 8.24 | 24 | 6.59 | 0.375 | 1 |
| A\*02 | 363 | 29.32 | 98 | 26.92 | 0.392 | 1 |
| A\*74 | 5 | 0.40 | 0 | 0 | 0.594 | 1 |
| A\*24 | 119 | 9.61 | 38 | 10.44 | 0.618 | 1 |
| A\*23 | 20 | 1.62 | 4 | 1.10 | 0.626 | 1 |
| A\*68 | 19 | 1.53 | 6 | 1.65 | 0.813 | 1 |
| A\*31 | 14 | 1.13 | 4 | 1.10 | 1 | 1 |
| A\*69 | 10 | 0.81 | 2 | 0.55 | 1 | 1 |

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| --- | --- | --- | --- |
| **HLA-B****locus** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **B\*40** | 11 | 0.89 | 12 | 3.30 | **0.00183** | **0.0493** |
| **B\*58** | 141 | 11.39 | 22 | 6.04 | **0.00221** | 0.0597 |
| **B\*55** | 40 | 3.23 | 2 | 0.55 | **0.00247** | 0.0666 |
| **B\*53** | 5 | 0.40 | 8 | 2.20 | **0.00287** | 0.0774 |
| B\*56 | 3 | 0.24 | 4 | 1.10 | 0.051 | 1 |
| B\*35 | 153 | 12.36 | 58 | 15.93 | 0.0784 | 1 |
| B\*18 | 315 | 25.44 | 76 | 20.88 | 0.0826 | 1 |
| B\*08 | 30 | 2.42 | 14 | 3.85 | 0.147 | 1 |
| B\*44 | 58 | 4.68 | 24 | 6.59 | 0.175 | 1 |
| B\*73 | 8 | 0.65 | 0 | 0 | 0.211 | 1 |
| B\*14 | 74 | 5.98 | 28 | 7.69 | 0.271 | 1 |
| B\*41 | 18 | 1.45 | 2 | 0.55 | 0.28 | 1 |
| B\*45 | 18 | 1.45 | 2 | 0.55 | 0.28 | 1 |
| B\*07 | 37 | 2.99 | 14 | 3.85 | 0.399 | 1 |
| B\*57 | 9 | 0.73 | 4 | 1.10 | 0.507 | 1 |
| B\*38 | 16 | 1.29 | 6 | 1.65 | 0.61 | 1 |
| B\*78 | 4 | 0.32 | 2 | 0.55 | 0.624 | 1 |
| B\*39 | 22 | 1.78 | 8 | 2.20 | 0.659 | 1 |
| B\*13 | 23 | 1.86 | 8 | 2.20 | 0.667 | 1 |
| B\*15 | 23 | 1.86 | 8 | 2.20 | 0.667 | 1 |
| B\*49 | 75 | 6.06 | 20 | 5.49 | 0.801 | 1 |
| B\*27 | 24 | 1.94 | 6 | 1.65 | 0.829 | 1 |
| B\*51 | 79 | 6.38 | 22 | 6.04 | 0.903 | 1 |
| B\*37 | 14 | 1.13 | 4 | 1.10 | 1 | 1 |
| B\*47 | 2 | 0.16 | 0 | 0 | 1 | 1 |
| B\*50 | 15 | 1.21 | 4 | 1.10 | 1 | 1 |
| B\*52 | 21 | 1.70 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-C****locus** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **C\*04** | 139 | 11.23 | 66 | 18.13 | **0.000904** | **0.0118** |
| **C\*07** | 369 | 29.81 | 88 | 24.18 | **0.0406** | 0.527 |
| **C\*16** | 34 | 2.75 | 18 | 4.95 | **0.0436** | 0.567 |
| **C\*12** | 77 | 6.22 | 34 | 9.34 | **0.0456** | 0.593 |
| C\*14 | 10 | 0.81 | 0 | 0 | 0.129 | 1 |
| C\*03 | 48 | 3.88 | 8 | 2.20 | 0.145 | 1 |
| C\*06 | 76 | 6.14 | 16 | 4.40 | 0.249 | 1 |
| C\*05 | 243 | 19.63 | 62 | 17.03 | 0.288 | 1 |
| C\*08 | 73 | 5.90 | 26 | 7.14 | 0.387 | 1 |
| C\*17 | 16 | 1.29 | 2 | 0.55 | 0.394 | 1 |
| C\*02 | 73 | 5.90 | 24 | 6.59 | 0.618 | 1 |
| C\*01 | 26 | 2.10 | 6 | 1.65 | 0.676 | 1 |
| C\*15 | 54 | 4.36 | 14 | 3.85 | 0.768 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-DRB1****locus** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **DRB1\*14** | 34 | 2.75 | 20 | 5.49 | **0.0193** | 0.251 |
| DRB1\*11 | 195 | 15.75 | 44 | 12.09 | 0.0941 | 1 |
| DRB1\*12 | 19 | 1.53 | 2 | 0.55 | 0.193 | 1 |
| DRB1\*07 | 68 | 5.49 | 14 | 3.85 | 0.227 | 1 |
| DRB1\*13 | 51 | 4.12 | 18 | 4.95 | 0.466 | 1 |
| DRB1\*08 | 23 | 1.86 | 4 | 1.10 | 0.486 | 1 |
| DRB1\*16 | 240 | 19.39 | 76 | 20.88 | 0.549 | 1 |
| DRB1\*01 | 104 | 8.40 | 34 | 9.34 | 0.595 | 1 |
| DRB1\*04 | 164 | 13.25 | 52 | 14.29 | 0.601 | 1 |
| DRB1\*03 | 272 | 21.97 | 82 | 22.53 | 0.829 | 1 |
| DRB1\*09 | 2 | 0.16 | 0 | 0 | 1 | 1 |
| DRB1\*10 | 23 | 1.86 | 6 | 1.65 | 1 | 1 |
| DRB1\*15 | 43 | 3.47 | 12 | 3.30 | 1 | 1 |

Cochran’s rule – claiming that a minimum expected frequency of 5 can be regarded as adequate in analysing tables with more than a single degree of freedom – was used to establish which HLA haplotypes had frequencies sufficiently high to allow for significant comparisons between the two groups of patients and controls.

If $N\_{i; ctr}$ and $N\_{i; pts}$ are the number of times the *i*th HLA haplotype is present in the groups of controls and patients, respectively, $N\_{ctr}=619$ (the number of controls), $N\_{pts}=182$ (the number of Covid-19 patients),$ N\_{tot}=N\_{ctr}+N\_{pts}=801 $and$ N\_{i}= N\_{i; ctr}+N\_{i; pts}$. The Cochran’s rule yielded the constraint $N\_{i}>5∙\frac{N\_{tot}}{N\_{pts}}=22.0$, i.e. only the HLA haplotypes present in more than 22 subjects, either Covid-19 patients or controls, were considered.

The HLA haplotypes satisfying the Cochran’s rule (with expected frequencies greater than 5) are listed in the Tables below.

For multiple comparisons between the two groups, the corrected P values (Pc) were computed by multiplying the P values obtained according to the two-tailed Fisher’s exact test by the number of tested HLA haplotypes. Pc values smaller than 0.05 were only obtained for the following HLA haplotypes:

HLA-A\*30, B\*14 [Pc = 0.006, OR = 4.02 (1.82 – 8.98)]

HLA-A\*02, B\*58 [Pc = 0.007, OR = 0.35 (0.17 – 0.65)]

HLA-A\*30, C\*08 [Pc = 0.025, OR = 3.76 (1.62 – 8.79)]

HLA-A\*02, C\*07 [Pc = 0.028, OR = 0.54 (0.36 – 0.79)]

HLA-A\*02, B\*58, C\*07 [Pc = 0.011, OR = 0.36 (0.18 – 0.67)]

HLA-A\*30, B\*14, C\*08 [Pc = 0.025, OR = 3.76 (1.62 – 8.79)]

HLA-A\*02, B\*58, DRB1\*03 [Pc = 0.016, OR = 0 (0 – 0.42)]

HLA-A\*02, B\*18, DRB1\*16 [Pc = 0.017, OR = 0.14 (0.02 – 0.55)]

HLA-A\*02, B\*58, C\*07, DRB1\*03 [Pc = 0.015, OR = 0 (0 – 0.44)].

The second most frequent HLA four-loci haplotype HLA-A\*02, B\*58, C\*07, DRB1\*16 in the Sardinian population yielded a difference between controls and patients of P <0.05 but the corrected P value lost significance:

HLA-A\*02, B\*58, C\*07, DRB1\*16 [P = 0.004, Pc = 0.103, OR = 0.40 (0.18 – 0.78)].

Other HLA haplotypes with P < 0.05 but with Pc higher than 0.05 are highlighted in bold type in the following Tables.

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -B****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*30** | **B\*14** | 14 | 1.13 | 16 | 4.40 | **0.000224** | **0.00606** |
| **A\*02** | **B\*58** | 109 | 8.80 | 12 | 3.30 | **0.000263** | **0.0071** |
| **A\*03** | **B\*35** | 24 | 1.94 | 18 | 4.95 | **0.00417** | 0.112 |
| **A\*30** | **B\*35** | 37 | 2.99 | 2 | 0.55 | **0.00576** | 0.156 |
| **A\*30** | **B\*18** | 174 | 14.05 | 32 | 8.79 | **0.0075** | 0.203 |
| **A\*02** | **B\*18** | 133 | 10.74 | 24 | 6.59 | **0.0207** | 0.559 |
| **A\*02** | **B\*44** | 28 | 2.26 | 16 | 4.40 | **0.0426** | 1 |
| **A\*01** | **B\*18** | 28 | 2.26 | 2 | 0.55 | **0.0443** | 1 |
| A\*24 | B\*58 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*30 | B\*58 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*02 | B\*35 | 56 | 4.52 | 24 | 6.59 | 0.131 | 1 |
| A\*02 | B\*51 | 55 | 4.44 | 10 | 2.75 | 0.174 | 1 |
| A\*32 | B\*35 | 26 | 2.10 | 12 | 3.30 | 0.237 | 1 |
| A\*32 | B\*18 | 50 | 4.04 | 20 | 5.49 | 0.244 | 1 |
| A\*11 | B\*35 | 37 | 2.99 | 14 | 3.85 | 0.399 | 1 |
| A\*33 | B\*14 | 38 | 3.07 | 8 | 2.20 | 0.476 | 1 |
| A\*01 | B\*58 | 22 | 1.78 | 4 | 1.10 | 0.482 | 1 |
| A\*11 | B\*18 | 23 | 1.86 | 4 | 1.10 | 0.486 | 1 |
| A\*24 | B\*18 | 45 | 3.63 | 16 | 4.40 | 0.533 | 1 |
| A\*02 | B\*14 | 28 | 2.26 | 10 | 2.75 | 0.561 | 1 |
| A\*01 | B\*08 | 21 | 1.70 | 4 | 1.10 | 0.63 | 1 |
| A\*03 | B\*18 | 22 | 1.78 | 8 | 2.20 | 0.659 | 1 |
| A\*30 | B\*51 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| A\*01 | B\*49 | 25 | 2.02 | 6 | 1.65 | 0.829 | 1 |
| A\*24 | B\*35 | 31 | 2.50 | 8 | 2.20 | 0.848 | 1 |
| A\*02 | B\*49 | 45 | 3.63 | 14 | 3.85 | 0.874 | 1 |
| A\*01 | B\*35 | 21 | 1.7 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -C****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*30** | **C\*08** | 13 | 1.05 | 14 | 3.85 | **0.000819** | **0.0254** |
| **A\*02** | **C\*07** | 209 | 16.88 | 36 | 9.89 | **0.000891** | **0.0276** |
| **A\*03** | **C\*04** | 21 | 1.70 | 16 | 4.40 | **0.00478** | 0.148 |
| **A\*30** | **C\*05** | 175 | 14.14 | 32 | 8.79 | **0.0075** | 0.232 |
| **A\*02** | **C\*04** | 50 | 4.04 | 26 | 7.14 | **0.0173** | 0.535 |
| **A\*11** | **C\*07** | 28 | 2.26 | 16 | 4.40 | **0.0426** | 1 |
| **A\*02** | **C\*02** | 48 | 3.88 | 6 | 1.65 | **0.0458** | 1 |
| A\*24 | C\*12 | 21 | 1.70 | 12 | 3.30 | 0.0896 | 1 |
| A\*30 | C\*06 | 30 | 2.42 | 4 | 1.10 | 0.149 | 1 |
| A\*32 | C\*02 | 19 | 1.53 | 10 | 2.75 | 0.176 | 1 |
| A\*11 | C\*04 | 36 | 2.91 | 16 | 4.40 | 0.178 | 1 |
| A\*01 | C\*07 | 70 | 5.65 | 14 | 3.85 | 0.228 | 1 |
| A\*24 | C\*05 | 28 | 2.26 | 12 | 3.30 | 0.256 | 1 |
| A\*30 | C\*04 | 35 | 2.83 | 6 | 1.65 | 0.259 | 1 |
| A\*24 | C\*07 | 57 | 4.60 | 12 | 3.30 | 0.308 | 1 |
| A\*02 | C\*16 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*30 | C\*02 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*03 | C\*07 | 34 | 2.75 | 6 | 1.65 | 0.338 | 1 |
| A\*02 | C\*12 | 29 | 2.34 | 12 | 3.30 | 0.344 | 1 |
| A\*30 | C\*07 | 63 | 5.09 | 14 | 3.85 | 0.403 | 1 |
| A\*32 | C\*05 | 26 | 2.10 | 10 | 2.75 | 0.428 | 1 |
| A\*24 | C\*04 | 32 | 2.58 | 6 | 1.65 | 0.432 | 1 |
| A\*33 | C\*08 | 38 | 3.07 | 8 | 2.20 | 0.476 | 1 |
| A\*01 | C\*04 | 21 | 1.70 | 8 | 2.20 | 0.506 | 1 |
| A\*02 | C\*08 | 28 | 2.26 | 10 | 2.75 | 0.561 | 1 |
| A\*32 | C\*07 | 58 | 4.68 | 20 | 5.49 | 0.579 | 1 |
| A\*30 | C\*12 | 17 | 1.37 | 6 | 1.65 | 0.625 | 1 |
| A\*02 | C\*06 | 28 | 2.26 | 6 | 1.65 | 0.679 | 1 |
| A\*02 | C\*15 | 24 | 1.94 | 8 | 2.20 | 0.831 | 1 |
| A\*02 | C\*05 | 89 | 7.19 | 26 | 7.14 | 1 | 1 |
| A\*11 | C\*05 | 21 | 1.70 | 6 | 1.65 | 1 | 1 |

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| --- | --- | --- | --- |
| **HLA-A, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*11** | **DRB1\*16** | 25 | 2.02 | 18 | 4.95 | **0.00481** | 0.168 |
| **A\*01** | **DRB1\*16** | 29 | 2.34 | 2 | 0.55 | **0.0288** | 1 |
| **A\*02** | **DRB1\*16** | 138 | 11.15 | 26 | 7.14 | **0.03** | 1 |
| **A\*30** | **DRB1\*03** | 158 | 12.76 | 32 | 8.79 | **0.0423** | 1 |
| **A\*30** | **DRB1\*01** | 19 | 1.53 | 12 | 3.30 | **0.0482** | 1 |
| A\*32 | DRB1\*16 | 57 | 4.60 | 26 | 7.14 | 0.06 | 1 |
| A\*30 | DRB1\*07 | 25 | 2.02 | 2 | 0.55 | 0.0628 | 1 |
| A\*02 | DRB1\*03 | 111 | 8.97 | 22 | 6.04 | 0.0837 | 1 |
| A\*32 | DRB1\*11 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*32 | DRB1\*01 | 18 | 1.45 | 10 | 2.75 | 0.111 | 1 |
| A\*02 | DRB1\*11 | 96 | 7.75 | 20 | 5.49 | 0.167 | 1 |
| A\*30 | DRB1\*11 | 46 | 3.72 | 8 | 2.20 | 0.187 | 1 |
| A\*02 | DRB1\*01 | 44 | 3.55 | 18 | 4.95 | 0.219 | 1 |
| A\*24 | DRB1\*04 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| A\*01 | DRB1\*11 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*03 | DRB1\*04 | 19 | 1.53 | 8 | 2.20 | 0.362 | 1 |
| A\*30 | DRB1\*04 | 40 | 3.23 | 8 | 2.20 | 0.383 | 1 |
| A\*03 | DRB1\*11 | 25 | 2.02 | 10 | 2.75 | 0.415 | 1 |
| A\*24 | DRB1\*03 | 31 | 2.5 | 12 | 3.30 | 0.46 | 1 |
| A\*24 | DRB1\*01 | 22 | 1.78 | 4 | 1.10 | 0.482 | 1 |
| A\*11 | DRB1\*03 | 20 | 1.62 | 8 | 2.20 | 0.494 | 1 |
| A\*11 | DRB1\*04 | 21 | 1.70 | 8 | 2.20 | 0.506 | 1 |
| A\*32 | DRB1\*04 | 21 | 1.70 | 8 | 2.20 | 0.506 | 1 |
| A\*02 | DRB1\*04 | 84 | 6.79 | 28 | 7.69 | 0.559 | 1 |
| A\*32 | DRB1\*03 | 33 | 2.67 | 12 | 3.30 | 0.588 | 1 |
| A\*02 | DRB1\*15 | 17 | 1.37 | 6 | 1.65 | 0.625 | 1 |
| A\*01 | DRB1\*04 | 28 | 2.26 | 6 | 1.65 | 0.679 | 1 |
| A\*11 | DRB1\*01 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| A\*02 | DRB1\*13 | 25 | 2.02 | 8 | 2.20 | 0.834 | 1 |
| A\*24 | DRB1\*16 | 38 | 3.07 | 10 | 2.75 | 0.862 | 1 |
| A\*24 | DRB1\*11 | 46 | 3.72 | 12 | 3.30 | 0.873 | 1 |
| A\*30 | DRB1\*16 | 53 | 4.28 | 16 | 4.40 | 0.884 | 1 |
| A\*01 | DRB1\*03 | 41 | 3.31 | 12 | 3.30 | 1 | 1 |
| A\*02 | DRB1\*07 | 28 | 2.26 | 8 | 2.20 | 1 | 1 |
| A\*33 | DRB1\*01 | 21 | 1.70 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-B, -C****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **B\*14** | **C\*05** | 12 | 0.97 | 12 | 3.30 | **0.00487** | 0.146 |
| **B\*58** | **C\*07** | 134 | 10.82 | 22 | 6.04 | **0.00642** | 0.193 |
| **B\*55** | **C\*03** | 33 | 2.67 | 2 | 0.55 | **0.013** | 0.389 |
| **B\*18** | **C\*08** | 17 | 1.37 | 12 | 3.30 | **0.0234** | 0.702 |
| **B\*18** | **C\*07** | 129 | 10.42 | 24 | 6.59 | **0.0327** | 0.98 |
| **B\*35** | **C\*04** | 117 | 9.45 | 48 | 13.19 | **0.0493** | 1 |
| B\*44 | C\*04 | 15 | 1.21 | 10 | 2.75 | 0.0515 | 1 |
| B\*58 | C\*05 | 26 | 2.10 | 2 | 0.55 | 0.0649 | 1 |
| B\*35 | C\*07 | 38 | 3.07 | 18 | 4.95 | 0.103 | 1 |
| B\*18 | C\*05 | 214 | 17.29 | 50 | 13.74 | 0.127 | 1 |
| B\*08 | C\*07 | 30 | 2.42 | 14 | 3.85 | 0.147 | 1 |
| B\*35 | C\*05 | 31 | 2.50 | 4 | 1.10 | 0.151 | 1 |
| B\*14 | C\*07 | 16 | 1.29 | 8 | 2.20 | 0.221 | 1 |
| B\*51 | C\*07 | 27 | 2.18 | 4 | 1.10 | 0.277 | 1 |
| B\*14 | C\*08 | 73 | 5.90 | 26 | 7.14 | 0.387 | 1 |
| B\*44 | C\*05 | 32 | 2.58 | 12 | 3.30 | 0.467 | 1 |
| B\*18 | C\*12 | 39 | 3.15 | 8 | 2.20 | 0.479 | 1 |
| B\*18 | C\*06 | 20 | 1.62 | 4 | 1.10 | 0.626 | 1 |
| B\*18 | C\*15 | 20 | 1.62 | 4 | 1.10 | 0.626 | 1 |
| B\*07 | C\*07 | 26 | 2.10 | 6 | 1.65 | 0.676 | 1 |
| B\*49 | C\*07 | 75 | 6.06 | 20 | 5.49 | 0.801 | 1 |
| B\*13 | C\*06 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| B\*35 | C\*15 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| B\*39 | C\*07 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| B\*52 | C\*12 | 18 | 1.45 | 6 | 1.65 | 0.807 | 1 |
| B\*58 | C\*04 | 18 | 1.45 | 6 | 1.65 | 0.807 | 1 |
| B\*18 | C\*04 | 32 | 2.58 | 8 | 2.20 | 0.849 | 1 |
| B\*18 | C\*02 | 21 | 1.70 | 6 | 1.65 | 1 | 1 |
| B\*35 | C\*12 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |
| B\*51 | C\*02 | 35 | 2.83 | 10 | 2.75 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-B, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **B\*18** | **DRB1\*11** | 84 | 6.79 | 10 | 2.75 | **0.00324** | 0.094 |
| **B\*58** | **DRB1\*16** | 102 | 8.24 | 16 | 4.40 | **0.012** | 0.347 |
| **B\*35** | **DRB1\*16** | 55 | 4.44 | 26 | 7.14 | **0.042** | 1 |
| B\*35 | DRB1\*14 | 15 | 1.21 | 10 | 2.75 | 0.0515 | 1 |
| B\*14 | DRB1\*16 | 16 | 1.29 | 10 | 2.75 | 0.0608 | 1 |
| B\*58 | DRB1\*04 | 26 | 2.10 | 2 | 0.55 | 0.0649 | 1 |
| B\*58 | DRB1\*03 | 43 | 3.47 | 6 | 1.65 | 0.0836 | 1 |
| B\*58 | DRB1\*11 | 21 | 1.70 | 2 | 0.55 | 0.134 | 1 |
| B\*35 | DRB1\*04 | 29 | 2.34 | 14 | 3.85 | 0.139 | 1 |
| B\*18 | DRB1\*04 | 48 | 3.88 | 8 | 2.20 | 0.145 | 1 |
| B\*18 | DRB1\*03 | 199 | 16.07 | 48 | 13.19 | 0.188 | 1 |
| B\*35 | DRB1\*01 | 31 | 2.50 | 14 | 3.85 | 0.205 | 1 |
| B\*49 | DRB1\*16 | 16 | 1.29 | 8 | 2.20 | 0.221 | 1 |
| B\*08 | DRB1\*03 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| B\*14 | DRB1\*03 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| B\*18 | DRB1\*13 | 25 | 2.02 | 4 | 1.10 | 0.37 | 1 |
| B\*49 | DRB1\*03 | 25 | 2.02 | 4 | 1.10 | 0.37 | 1 |
| B\*51 | DRB1\*11 | 41 | 3.31 | 8 | 2.20 | 0.386 | 1 |
| B\*14 | DRB1\*01 | 43 | 3.47 | 16 | 4.40 | 0.429 | 1 |
| B\*49 | DRB1\*04 | 49 | 3.96 | 18 | 4.95 | 0.456 | 1 |
| B\*35 | DRB1\*03 | 30 | 2.42 | 6 | 1.65 | 0.545 | 1 |
| B\*18 | DRB1\*01 | 27 | 2.18 | 10 | 2.75 | 0.552 | 1 |
| B\*51 | DRB1\*03 | 21 | 1.70 | 4 | 1.10 | 0.63 | 1 |
| B\*35 | DRB1\*11 | 56 | 4.52 | 14 | 3.85 | 0.663 | 1 |
| B\*44 | DRB1\*16 | 18 | 1.45 | 6 | 1.65 | 0.807 | 1 |
| B\*51 | DRB1\*04 | 24 | 1.94 | 6 | 1.65 | 0.829 | 1 |
| B\*18 | DRB1\*16 | 87 | 7.03 | 24 | 6.59 | 0.907 | 1 |
| B\*49 | DRB1\*11 | 23 | 1.86 | 6 | 1.65 | 1 | 1 |
| B\*51 | DRB1\*16 | 22 | 1.78 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-C, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **C\*04** | **DRB1\*16** | 40 | 3.23 | 24 | 6.59 | **0.00592** | 0.19 |
| **C\*04** | **DRB1\*04** | 32 | 2.58 | 20 | 5.49 | **0.0105** | 0.336 |
| **C\*07** | **DRB1\*11** | 74 | 5.98 | 10 | 2.75 | **0.0154** | 0.492 |
| **C\*05** | **DRB1\*01** | 20 | 1.62 | 14 | 3.85 | **0.0204** | 0.653 |
| **C\*06** | **DRB1\*04** | 29 | 2.34 | 2 | 0.55 | **0.0288** | 0.922 |
| C\*05 | DRB1\*04 | 34 | 2.75 | 4 | 1.10 | 0.0779 | 1 |
| C\*07 | DRB1\*16 | 158 | 12.76 | 34 | 9.34 | 0.0814 | 1 |
| C\*15 | DRB1\*04 | 23 | 1.86 | 2 | 0.55 | 0.0919 | 1 |
| C\*12 | DRB1\*16 | 17 | 1.37 | 10 | 2.75 | 0.101 | 1 |
| C\*12 | DRB1\*11 | 37 | 2.99 | 16 | 4.40 | 0.185 | 1 |
| C\*07 | DRB1\*03 | 109 | 8.80 | 24 | 6.59 | 0.196 | 1 |
| C\*08 | DRB1\*16 | 16 | 1.29 | 8 | 2.20 | 0.221 | 1 |
| C\*07 | DRB1\*04 | 93 | 7.51 | 34 | 9.34 | 0.27 | 1 |
| C\*08 | DRB1\*03 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| C\*02 | DRB1\*16 | 33 | 2.67 | 14 | 3.85 | 0.287 | 1 |
| C\*05 | DRB1\*11 | 42 | 3.39 | 8 | 2.20 | 0.305 | 1 |
| C\*08 | DRB1\*01 | 42 | 3.39 | 16 | 4.40 | 0.343 | 1 |
| C\*02 | DRB1\*03 | 19 | 1.53 | 8 | 2.20 | 0.362 | 1 |
| C\*06 | DRB1\*03 | 24 | 1.94 | 4 | 1.10 | 0.366 | 1 |
| C\*06 | DRB1\*07 | 24 | 1.94 | 4 | 1.10 | 0.366 | 1 |
| C\*05 | DRB1\*03 | 192 | 15.51 | 50 | 13.74 | 0.454 | 1 |
| C\*07 | DRB1\*01 | 38 | 3.07 | 8 | 2.20 | 0.476 | 1 |
| C\*06 | DRB1\*11 | 17 | 1.37 | 6 | 1.65 | 0.625 | 1 |
| C\*12 | DRB1\*03 | 17 | 1.37 | 6 | 1.65 | 0.625 | 1 |
| C\*04 | DRB1\*03 | 26 | 2.10 | 6 | 1.65 | 0.676 | 1 |
| C\*07 | DRB1\*07 | 26 | 2.10 | 6 | 1.65 | 0.676 | 1 |
| C\*02 | DRB1\*11 | 25 | 2.02 | 6 | 1.65 | 0.829 | 1 |
| C\*07 | DRB1\*13 | 24 | 1.94 | 8 | 2.20 | 0.831 | 1 |
| C\*04 | DRB1\*11 | 51 | 4.12 | 14 | 3.85 | 0.881 | 1 |
| C\*04 | DRB1\*01 | 34 | 2.75 | 10 | 2.75 | 1 | 1 |
| C\*05 | DRB1\*16 | 55 | 4.44 | 16 | 4.40 | 1 | 1 |
| C\*15 | DRB1\*16 | 21 | 1.70 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -B, -C****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*02** | **B\*58** | **C\*07** | 107 | 8.64 | 12 | 3.30 | **0.00037** | **0.0111** |
| **A\*30** | **B\*14** | **C\*08** | 13 | 1.05 | 14 | 3.85 | **0.000819** | **0.0246** |
| **A\*02** | **B\*18** | **C\*07** | 76 | 6.14 | 8 | 2.20 | **0.00193** | 0.058 |
| **A\*30** | **B\*35** | **C\*05** | 25 | 2.02 | 0 | 0 | **0.00273** | 0.0818 |
| **A\*03** | **B\*35** | **C\*04** | 21 | 1.70 | 16 | 4.40 | **0.00478** | 0.143 |
| **A\*30** | **B\*18** | **C\*07** | 47 | 3.80 | 4 | 1.10 | **0.00973** | 0.292 |
| **A\*30** | **B\*18** | **C\*05** | 171 | 13.81 | 32 | 8.79 | **0.0119** | 0.356 |
| **A\*30** | **B\*35** | **C\*04** | 30 | 2.42 | 2 | 0.55 | **0.0301** | 0.904 |
| A\*02 | B\*35 | C\*04 | 42 | 3.39 | 20 | 5.49 | 0.0874 | 1 |
| A\*24 | B\*58 | C\*07 | 23 | 1.86 | 2 | 0.55 | 0.0919 | 1 |
| A\*01 | B\*18 | C\*07 | 21 | 1.70 | 2 | 0.55 | 0.134 | 1 |
| A\*30 | B\*58 | C\*07 | 21 | 1.70 | 2 | 0.55 | 0.134 | 1 |
| A\*02 | B\*51 | C\*02 | 30 | 2.42 | 4 | 1.10 | 0.149 | 1 |
| A\*24 | B\*18 | C\*07 | 20 | 1.62 | 10 | 2.75 | 0.185 | 1 |
| A\*24 | B\*35 | C\*04 | 26 | 2.10 | 4 | 1.10 | 0.274 | 1 |
| A\*11 | B\*35 | C\*04 | 35 | 2.83 | 14 | 3.85 | 0.304 | 1 |
| A\*02 | B\*44 | C\*05 | 18 | 1.45 | 8 | 2.20 | 0.345 | 1 |
| A\*02 | B\*18 | C\*05 | 79 | 6.38 | 18 | 4.95 | 0.381 | 1 |
| A\*32 | B\*18 | C\*05 | 24 | 1.94 | 10 | 2.75 | 0.406 | 1 |
| A\*32 | B\*18 | C\*07 | 31 | 2.50 | 12 | 3.30 | 0.46 | 1 |
| A\*33 | B\*14 | C\*08 | 38 | 3.07 | 8 | 2.20 | 0.476 | 1 |
| A\*01 | B\*58 | C\*07 | 22 | 1.78 | 4 | 1.10 | 0.482 | 1 |
| A\*02 | B\*51 | C\*07 | 22 | 1.78 | 4 | 1.10 | 0.482 | 1 |
| A\*02 | B\*35 | C\*07 | 20 | 1.62 | 8 | 2.20 | 0.494 | 1 |
| A\*02 | B\*14 | C\*08 | 28 | 2.26 | 10 | 2.75 | 0.561 | 1 |
| A\*01 | B\*08 | C\*07 | 21 | 1.70 | 4 | 1.10 | 0.63 | 1 |
| A\*01 | B\*49 | C\*07 | 25 | 2.02 | 6 | 1.65 | 0.829 | 1 |
| A\*24 | B\*18 | C\*05 | 24 | 1.94 | 8 | 2.20 | 0.831 | 1 |
| A\*02 | B\*49 | C\*07 | 45 | 3.63 | 14 | 3.85 | 0.874 | 1 |
| A\*01 | B\*35 | C\*04 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -B, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*02** | **B\*58** | **DRB1\*03** | 31 | 2.50 | 0 | 0 | **0.000679** | **0.0163** |
| **A\*02** | **B\*18** | **DRB1\*16** | 46 | 3.72 | 2 | 0.55 | **0.00069** | **0.0166** |
| **A\*02** | **B\*58** | **DRB1\*16** | 82 | 6.62 | 10 | 2.75 | **0.00447** | 0.107 |
| **A\*30** | **B\*18** | **DRB1\*11** | 34 | 2.75 | 2 | 0.55 | **0.00861** | 0.207 |
| **A\*30** | **B\*18** | **DRB1\*03** | 154 | 12.44 | 30 | 8.24 | **0.0311** | 0.746 |
| **A\*02** | **B\*18** | **DRB1\*04** | 28 | 2.26 | 2 | 0.55 | **0.0443** | 1 |
| **A\*32** | **B\*18** | **DRB1\*16** | 29 | 2.34 | 16 | 4.40 | **0.0462** | 1 |
| A\*02 | B\*18 | DRB1\*11 | 43 | 3.47 | 6 | 1.65 | 0.0836 | 1 |
| A\*02 | B\*58 | DRB1\*04 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*02 | B\*51 | DRB1\*11 | 29 | 2.34 | 4 | 1.10 | 0.206 | 1 |
| A\*02 | B\*14 | DRB1\*01 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*02 | B\*35 | DRB1\*16 | 30 | 2.42 | 12 | 3.30 | 0.354 | 1 |
| A\*02 | B\*49 | DRB1\*04 | 30 | 2.42 | 12 | 3.30 | 0.354 | 1 |
| A\*02 | B\*18 | DRB1\*03 | 76 | 6.14 | 18 | 4.95 | 0.448 | 1 |
| A\*02 | B\*35 | DRB1\*11 | 22 | 1.78 | 4 | 1.10 | 0.482 | 1 |
| A\*32 | B\*18 | DRB1\*03 | 27 | 2.18 | 10 | 2.75 | 0.552 | 1 |
| A\*01 | B\*49 | DRB1\*04 | 21 | 1.70 | 4 | 1.10 | 0.63 | 1 |
| A\*01 | B\*08 | DRB1\*03 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| A\*32 | B\*35 | DRB1\*16 | 18 | 1.45 | 6 | 1.65 | 0.807 | 1 |
| A\*30 | B\*18 | DRB1\*16 | 39 | 3.15 | 10 | 2.75 | 0.863 | 1 |
| A\*02 | B\*51 | DRB1\*04 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |
| A\*24 | B\*18 | DRB1\*03 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |
| A\*24 | B\*18 | DRB1\*11 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |
| A\*33 | B\*14 | DRB1\*01 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -C, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*11** | **C\*07** | **DRB1\*16** | 13 | 1.05 | 12 | 3.30 | **0.00598** | 0.156 |
| **A\*30** | **C\*05** | **DRB1\*11** | 35 | 2.83 | 2 | 0.55 | **0.00866** | 0.225 |
| **A\*02** | **C\*07** | **DRB1\*03** | 57 | 4.60 | 6 | 1.65 | **0.00869** | 0.226 |
| **A\*30** | **C\*05** | **DRB1\*03** | 155 | 12.52 | 30 | 8.24 | **0.025** | 0.651 |
| **A\*02** | **C\*07** | **DRB1\*16** | 106 | 8.56 | 18 | 4.95 | **0.0251** | 0.654 |
| A\*01 | C\*07 | DRB1\*16 | 25 | 2.02 | 2 | 0.55 | 0.0628 | 1 |
| A\*30 | C\*07 | DRB1\*03 | 44 | 3.55 | 6 | 1.65 | 0.0846 | 1 |
| A\*02 | C\*07 | DRB1\*11 | 50 | 4.04 | 8 | 2.20 | 0.111 | 1 |
| A\*02 | C\*05 | DRB1\*16 | 30 | 2.42 | 4 | 1.1 | 0.149 | 1 |
| A\*32 | C\*05 | DRB1\*03 | 21 | 1.70 | 10 | 2.75 | 0.198 | 1 |
| A\*24 | C\*12 | DRB1\*11 | 15 | 1.21 | 8 | 2.20 | 0.206 | 1 |
| A\*24 | C\*07 | DRB1\*16 | 27 | 2.18 | 4 | 1.10 | 0.277 | 1 |
| A\*02 | C\*04 | DRB1\*16 | 23 | 1.86 | 10 | 2.75 | 0.296 | 1 |
| A\*02 | C\*08 | DRB1\*01 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*32 | C\*07 | DRB1\*16 | 37 | 2.99 | 14 | 3.85 | 0.399 | 1 |
| A\*02 | C\*07 | DRB1\*01 | 23 | 1.86 | 4 | 1.10 | 0.486 | 1 |
| A\*30 | C\*07 | DRB1\*16 | 29 | 2.34 | 6 | 1.65 | 0.542 | 1 |
| A\*02 | C\*05 | DRB1\*03 | 72 | 5.82 | 18 | 4.95 | 0.605 | 1 |
| A\*24 | C\*05 | DRB1\*03 | 22 | 1.78 | 8 | 2.2 | 0.659 | 1 |
| A\*02 | C\*07 | DRB1\*04 | 60 | 4.85 | 16 | 4.4 | 0.781 | 1 |
| A\*02 | C\*04 | DRB1\*11 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| A\*30 | C\*07 | DRB1\*04 | 19 | 1.53 | 6 | 1.65 | 0.813 | 1 |
| A\*01 | C\*07 | DRB1\*04 | 25 | 2.02 | 6 | 1.65 | 0.829 | 1 |
| A\*01 | C\*07 | DRB1\*03 | 34 | 2.75 | 10 | 2.75 | 1 | 1 |
| A\*30 | C\*05 | DRB1\*16 | 36 | 2.91 | 10 | 2.75 | 1 | 1 |
| A\*33 | C\*08 | DRB1\*01 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-B, -C, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **B\*18** | **C\*07** | **DRB1\*11** | 39 | 3.15 | 2 | 0.55 | **0.00382** | 0.111 |
| **B\*35** | **C\*04** | **DRB1\*16** | 36 | 2.91 | 22 | 6.04 | **0.00966** | 0.28 |
| **B\*58** | **C\*07** | **DRB1\*16** | 101 | 8.16 | 16 | 4.40 | **0.0157** | 0.454 |
| **B\*18** | **C\*05** | **DRB1\*11** | 40 | 3.23 | 4 | 1.10 | **0.0278** | 0.807 |
| B\*18 | C\*05 | DRB1\*01 | 16 | 1.29 | 10 | 2.75 | 0.0608 | 1 |
| B\*18 | C\*07 | DRB1\*03 | 64 | 5.17 | 10 | 2.75 | 0.0636 | 1 |
| B\*18 | C\*05 | DRB1\*04 | 26 | 2.10 | 2 | 0.55 | 0.0649 | 1 |
| B\*58 | C\*07 | DRB1\*04 | 26 | 2.10 | 2 | 0.55 | 0.0649 | 1 |
| B\*35 | C\*05 | DRB1\*03 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| B\*58 | C\*07 | DRB1\*03 | 39 | 3.15 | 6 | 1.65 | 0.15 | 1 |
| B\*35 | C\*04 | DRB1\*04 | 24 | 1.94 | 12 | 3.30 | 0.156 | 1 |
| B\*35 | C\*07 | DRB1\*16 | 25 | 2.02 | 12 | 3.30 | 0.165 | 1 |
| B\*14 | C\*08 | DRB1\*16 | 16 | 1.29 | 8 | 2.20 | 0.221 | 1 |
| B\*49 | C\*07 | DRB1\*16 | 16 | 1.29 | 8 | 2.20 | 0.221 | 1 |
| B\*08 | C\*07 | DRB1\*03 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| B\*14 | C\*08 | DRB1\*03 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| B\*18 | C\*07 | DRB1\*16 | 57 | 4.60 | 12 | 3.30 | 0.308 | 1 |
| B\*14 | C\*08 | DRB1\*01 | 42 | 3.39 | 16 | 4.40 | 0.343 | 1 |
| B\*49 | C\*07 | DRB1\*03 | 25 | 2.02 | 4 | 1.10 | 0.37 | 1 |
| B\*18 | C\*05 | DRB1\*03 | 188 | 15.19 | 48 | 13.19 | 0.4 | 1 |
| B\*49 | C\*07 | DRB1\*04 | 49 | 3.96 | 18 | 4.95 | 0.456 | 1 |
| B\*18 | C\*07 | DRB1\*04 | 36 | 2.91 | 8 | 2.20 | 0.585 | 1 |
| B\*35 | C\*04 | DRB1\*03 | 21 | 1.70 | 4 | 1.10 | 0.63 | 1 |
| B\*18 | C\*12 | DRB1\*11 | 27 | 2.18 | 6 | 1.65 | 0.676 | 1 |
| B\*35 | C\*04 | DRB1\*01 | 29 | 2.34 | 10 | 2.75 | 0.699 | 1 |
| B\*35 | C\*04 | DRB1\*11 | 48 | 3.88 | 12 | 3.30 | 0.753 | 1 |
| B\*51 | C\*02 | DRB1\*11 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| B\*18 | C\*05 | DRB1\*16 | 48 | 3.88 | 14 | 3.85 | 1 | 1 |
| B\*49 | C\*07 | DRB1\*11 | 23 | 1.86 | 6 | 1.65 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A, -B, -C, -DR****haplotypes** | **Controls****(1238 alleles)** | **Patients****(364 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*02** | **B\*58** | **C\*07** | **DRB1\*03** | 30 | 2.42 | 0 | 0 | **0.000629** | **0.0145** |
| **A\*02** | **B\*58** | **C\*07** | **DRB1\*16** | 82 | 6.62 | 10 | 2.75 | **0.00447** | 0.103 |
| **A\*30** | **B\*18** | **C\*05** | **DRB1\*11** | 34 | 2.75 | 2 | 0.55 | **0.00861** | 0.198 |
| **A\*02** | **B\*18** | **C\*07** | **DRB1\*16** | 33 | 2.67 | 2 | 0.55 | **0.013** | 0.298 |
| **A\*30** | **B\*18** | **C\*07** | **DRB1\*03** | 42 | 3.39 | 4 | 1.10 | **0.0195** | 0.448 |
| **A\*30** | **B\*18** | **C\*05** | **DRB1\*03** | 154 | 12.44 | 30 | 8.24 | **0.0311** | 0.715 |
| A\*02 | B\*18 | C\*07 | DRB1\*11 | 26 | 2.10 | 2 | 0.55 | 0.0649 | 1 |
| A\*02 | B\*18 | C\*05 | DRB1\*16 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*02 | B\*58 | C\*07 | DRB1\*04 | 24 | 1.94 | 2 | 0.55 | 0.0946 | 1 |
| A\*02 | B\*18 | C\*07 | DRB1\*04 | 22 | 1.78 | 2 | 0.55 | 0.137 | 1 |
| A\*02 | B\*18 | C\*07 | DRB1\*03 | 30 | 2.42 | 4 | 1.10 | 0.149 | 1 |
| A\*02 | B\*35 | C\*04 | DRB1\*16 | 20 | 1.62 | 10 | 2.75 | 0.185 | 1 |
| A\*32 | B\*18 | C\*05 | DRB1\*03 | 21 | 1.7 | 10 | 2.75 | 0.198 | 1 |
| A\*32 | B\*18 | C\*07 | DRB1\*16 | 22 | 1.78 | 10 | 2.75 | 0.285 | 1 |
| A\*02 | B\*14 | C\*08 | DRB1\*01 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*02 | B\*35 | C\*07 | DRB1\*16 | 17 | 1.37 | 8 | 2.20 | 0.333 | 1 |
| A\*02 | B\*49 | C\*07 | DRB1\*04 | 30 | 2.42 | 12 | 3.30 | 0.354 | 1 |
| A\*01 | B\*49 | C\*07 | DRB1\*04 | 21 | 1.7 | 4 | 1.10 | 0.63 | 1 |
| A\*02 | B\*18 | C\*05 | DRB1\*03 | 69 | 5.57 | 18 | 4.95 | 0.695 | 1 |
| A\*01 | B\*08 | C\*07 | DRB1\*03 | 19 | 1.53 | 4 | 1.10 | 0.802 | 1 |
| A\*24 | B\*18 | C\*05 | DRB1\*03 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |
| A\*30 | B\*18 | C\*05 | DRB1\*16 | 36 | 2.91 | 10 | 2.75 | 1 | 1 |
| A\*33 | B\*14 | C\*08 | DRB1\*01 | 20 | 1.62 | 6 | 1.65 | 1 | 1 |

**HLA alleles and haplotypes in patients with mild (Group A) and severe symptoms (Group S).**

The group of 182 patients infected with SARS-CoV-2 was stratified into a group of 143 pauci-symptomatic patients or affected by mild symptoms (Group A) and a group of 39 patients with moderate or severe symptoms (Group S). The Tables in the following pages list the HLA allele frequencies in the two cohorts of patients with mild and severe symptoms. For multiple comparisons, the corrected P values (Pc) were obtained by multiplying the P values calculated according to the two-tailed Fisher’s exact test by the number of tested alleles (17 for HLA-A, 25 for HLA-B, 12 for HLA-C and HLA-DR).

The only alleles with Pc < 0.05, corresponding to statistically significant comparisons, were:

HLA-A\*23 (Pc = 0.034, OR > 2.5) and HLA-DRB1\*08 (Pc = 0.024, OR > 2.5).

Other alleles with P < 0.05 but with Pc higher than the significance threshold are highlighted in bold type in the following Tables.

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-A****locus** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **A\*23** | 0 | 0 | 4 | 5.1 | **0.002** | **0.034** |
| **A\*69** | 0 | 0 | 2 | 2.6 | **0.045** | 0.765 |
| A\*01 | 21 | 7.3 | 2 | 2.6 | 0.187 | 1 |
| A\*31 | 2 | 0.7 | 2 | 2.6 | 0.202 | 1 |
| A\*32 | 28 | 9.8 | 10 | 12.8 | 0.411 | 1 |
| A\*11 | 32 | 11.2 | 6 | 7.7 | 0.530 | 1 |
| A\*24 | 32 | 11.2 | 6 | 7.7 | 0.530 | 1 |
| A\*29 | 4 | 1.4 | 0 | 0 | 0.582 | 1 |
| A\*68 | 4 | 1.4 | 2 | 2.6 | 0.613 | 1 |
| A\*03 | 19 | 6.6 | 4 | 5.1 | 0.795 | 1 |
| A\*02 | 79 | 27.6 | 23 | 29.5 | 0.778 | 1 |
| A\*25 | 2 | 0.7 | 0 | 0 | 1 | 1 |
| A\*26 | 7 | 2.4 | 2 | 2.6 | 1 | 1 |
| A\*30 | 45 | 15.7 | 12 | 15.4 | 1 | 1 |
| A\*33 | 7 | 2.4 | 2 | 2.6 | 1 | 1 |
| A\*66 | 2 | 0.7 | 0 | 0 | 1 | 1 |
| A\*80 | 2 | 0.7 | 0 | 0 | 1 | 1 |

|  |  |  |  |
| --- | --- | --- | --- |
| **HLA-B****locus** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **B\*07** | 7 | 2.4 | 6 | 7.7 | **0.038** | 0.950 |
| **B\*40** | 7 | 2.4 | 6 | 7.7 | **0.038** | 0.950 |
| B\*15 | 4 | 1.4 | 4 | 5.1 | 0.068 | 1 |
| B\*53 | 4 | 1.4 | 4 | 5.1 | 0.068 | 1 |
| B\*51 | 21 | 7.3 | 2 | 2.6 | 0.187 | 1 |
| B\*39 | 9 | 3.1 | 0 | 0 | 0.214 | 1 |
| B\*37 | 2 | 0.7 | 2 | 2.6 | 0.202 | 1 |
| B\*49 | 19 | 6.6 | 2 | 2.6 | 0.271 | 1 |
| B\*14 | 19 | 6.6 | 8 | 10.3 | 0.328 | 1 |
| B\*38 | 7 | 2.4 | 0 | 0 | 0.354 | 1 |
| B\*52 | 7 | 2.4 | 0 | 0 | 0.354 | 1 |
| B\*08 | 11 | 3.8 | 4 | 5.1 | 0.537 | 1 |
| B\*27 | 4 | 1.4 | 0 | 0 | 0.582 | 1 |
| B\*50 | 4 | 1.4 | 0 | 0 | 0.582 | 1 |
| B\*56 | 4 | 1.4 | 0 | 0 | 0.582 | 1 |
| B\*57 | 4 | 1.4 | 0 | 0 | 0.582 | 1 |
| B\*58 | 19 | 6.6 | 4 | 5.1 | 0.795 | 1 |
| B\*18 | 58 | 20.3 | 16 | 20.5 | 1 | 1 |
| B\*13 | 7 | 2.4 | 2 | 2.6 | 1 | 1 |
| B\*35 | 45 | 15.7 | 12 | 15.4 | 1 | 1 |
| B\*41 | 2 | 0.7 | 0 | 0 | 1 | 1 |
| B\*44 | 17 | 5.9 | 4 | 5.1 | 1 | 1 |
| B\*45 | 2 | 0.7 | 0 | 0 | 1 | 1 |
| B\*55 | 2 | 0.7 | 0 | 0 | 1 | 1 |
| B\*78 | 2 | 0.7 | 0 | 0 | 1 | 1 |

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| --- | --- | --- | --- |
| **HLA-C****locus** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **C\*12** | 34 | 11.9 | 2 | 2.6 | **0.010** | 0.120 |
| C\*03 | 4 | 1.4 | 4 | 5.1 | 0.068 | 0.816 |
| C\*08 | 17 | 5.9 | 8 | 10.3 | 0.206 | 1 |
| C\*02 | 19 | 6.6 | 2 | 2.6 | 0.271 | 1 |
| C\*05 | 45 | 15.7 | 16 | 20.5 | 0.310 | 1 |
| C\*15 | 9 | 3.1 | 4 | 5.1 | 0.488 | 1 |
| C\*01 | 7 | 2.4 | 0 | 0 | 0.354 | 1 |
| C\*07 | 68 | 23.8 | 23 | 29.5 | 0.305 | 1 |
| C\*06 | 15 | 5.2 | 2 | 2.6 | 0.544 | 1 |
| C\*16 | 15 | 5.2 | 2 | 2.6 | 0.544 | 1 |
| C\*04 | 51 | 17.8 | 14 | 17.9 | 1 | 1 |
| C\*17 | 2 | 0.7 | 0 | 0 | 1 | 1 |

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| --- | --- | --- | --- |
| **HLA-DRB1****locus** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| **DRB1\*08** | 0 | 0 | 4 | 5.1 | **0.002** | **0.024** |
| **DRB1\*11** | 43 | 15.0 | 4 | 5.1 | **0.021** | 0.252 |
| **DRB1\*04** | 32 | 11.2 | 16 | 20.5 | **0.038** | 0.456 |
| DRB1\*01 | 23 | 8.0 | 10 | 12.8 | 0.189 | 1 |
| DRB1\*10 | 7 | 2.4 | 0 | 0 | 0.354 | 1 |
| DRB1\*13 | 17 | 5.9 | 2 | 2.6 | 0.387 | 1 |
| DRB1\*14 | 17 | 5.9 | 2 | 2.6 | 0.387 | 1 |
| DRB1\*16 | 55 | 19.2 | 18 | 23.1 | 0.523 | 1 |
| DRB1\*07 | 13 | 4.5 | 2 | 2.6 | 0.747 | 1 |
| DRB1\*03 | 66 | 23.1 | 16 | 20.5 | 0.760 | 1 |
| DRB1\*15 | 11 | 3.8 | 2 | 2.6 | 0.743 | 1 |
| DRB1\*12 | 2 | 0.7 | 0 | 0 | 1 | 1 |

The HLA haplotypes satisfying the Cochran’s rule (with expected frequencies greater than 5) are listed in the Tables below. No statistically significant differences were observed between the two groups of patients with mild or moderate and severe symptoms.

|  |  |  |  |
| --- | --- | --- | --- |
| **Two-loci HLA** **haplotypes** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| A\*30 | B\*18 | 23 | 8.0 | 8 | 10.3 | 0.500 | 1 |
| A\*02 | B\*18 | 21 | 7.3 | 4 | 5.1 | 0.619 | 1 |
| A\*02 | B\*35 | 19 | 6.6 | 6 | 7.7 | 0.801 | 1 |
| A\*02 | C\*05 | 19 | 6.6 | 8 | 10.3 | 0.328 | 1 |
| A\*30 | C\*05 | 23 | 8.0 | 8 | 10.3 | 0.500 | 1 |
| A\*02 | C\*04 | 21 | 7.3 | 6 | 7.7 | 1 | 1 |
| A\*02 | C\*07 | 30 | 10.5 | 8 | 10.3 | 1 | 1 |
| A\*30 | DRB1\*03 | 21 | 7.3 | 10 | 12.8 | 0.167 | 0.668 |
| A\*02 | DRB1\*04 | 19 | 6.6 | 8 | 10.3 | 0.328 | 1 |
| A\*02 | DRB1\*16 | 19 | 6.6 | 8 | 10.3 | 0.328 | 1 |
| A\*32 | DRB1\*16 | 19 | 6.6 | 6 | 7.7 | 0.801 | 1 |
| B\*35 | C\*04 | 40 | 14.0 | 6 | 7.7 | 0.178 | 0.534 |
| B\*14 | C\*08 | 17 | 5.9 | 8 | 10.3 | 0.206 | 0.618 |
| B\*18 | C\*05 | 36 | 12.6 | 12 | 15.4 | 0.571 | 1 |
| B\*18 | DRB1\*03 | 34 | 11.9 | 12 | 15.4 | 0.442 | 0.442 |
| C\*07 | DRB1\*04 | 23 | 8.0 | 10 | 12.8 | 0.189 | 0.567 |
| C\*07 | DRB1\*16 | 26 | 9.1 | 10 | 12.8 | 0.391 | 1 |
| C\*05 | DRB1\*03 | 36 | 12.6 | 12 | 15.4 | 0.571 | 1 |

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| --- | --- | --- | --- |
| **Three-loci HLA** **haplotypes** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| A\*30 | B\*18 | C\*05 | 23 | 8.0 | 8 | 10.3 | 0.500 | 0.500 |
| A\*30 | B\*18 | DRB1\*03 | 21 | 7.3 | 8 | 10.3 | 0.478 | 0.478 |
| A\*30 | C\*05 | DRB1\*03 | 21 | 7.3 | 8 | 10.3 | 0.478 | 0.478 |
| B\*18 | C\*05 | DRB1\*03 | 34 | 11.9 | 12 | 15.4 | 0.442 | 0.442 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Four-loci HLA** **haplotypes** | **Group A****(286 alleles)** | **Group S****(78 alleles)** | **P values** |
| **n** | **f (%)** | **n** | **f (%)** | **P** | **Pc** |
| A\*30 | B\*18 | C\*05 | DRB1\*03 | 21 | 7.3 | 8 | 10.3 | 0.478 | 0.478 |