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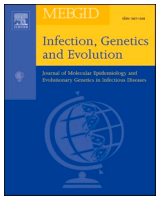

# Association of human leukocyte antigen class I and class II alleles and haplotypes in COVID-19 infection in a western Indian population

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*Dear Editor,*

In December 2022 an interesting and potentially important review article published in this journal entitled "Genome-wide association studies of COVID-19: Connecting the dots", emphasized the role of host genetic variants and SARS-CoV-2 infection outcome (Ferreira et al., 2022. Highly polymorphic human leukocyte antigen (HLA) alleles is one of the major host genetic factor, also known to be responsible for susceptibility or protection towards infectious diseases (Lorente et al., 2021). The current study was undertaken to assess the role of host genetic factors towards the resistance and/or susceptibility to COVID-19 infection. We have genotyped HLA class I and II loci in a case-control study of 235 COVID-19 patients and 228 COVID-19 negative healthy controls from Maharashtra, India using a polymerase chain reaction-sequence specific primer (PCR-SSP) kit following the manufacturer's instructions (Olerup SSP HLA-A-B-C and Olerup SSP DQ-DR Combi trays of low resolution, CareDx, California, USA). The sequence specific primers along with the internal control primers were included in the combi-trays, to prevent false negative results that could arise due to the PCR. Molecular typing for HLA class II was carried out in 82 severe, 134 mild patients and 228 and 220 healthy controls for DQ and DR respectively. Similarly HLA class I typing was carried out in 101 severe, 113 mild patients and 225 healthy controls. For statistical analysis, the alleles were interpreted on the Helmberg-SCORE 5 software. Quantitative variables such as allele frequencies were estimated by direct genotypic counts and were expressed as percentage of total number of alleles (2n) in each group. The allele frequencies among the study groups were compared using 2 × 2 contingency table in the OpenEpi software (version 3.01, Dean AG, Sullivan KM, Soe MM. OpenEpi: Open-Source Epidemiologic Statistics for Public Health, Version. www.OpenEpi.com). The results were considered significant when $p$ value was $\leq 0.05$ using Chi-square test with Yates correction / Fisher exact test. Bonferroni correction was further applied to determine the corrected $p$ value. The $p$-values, odds ratios (OR), 95% confidence interval and relative risk were estimated using the same software. The multi-locus analysis to estimate HLA haplotype frequencies was performed using PyPopwin32–0.7.0 software. Haplotype frequencies of >5% in either group were only considered (Lancaster et al., 2007). Only Bonferroni corrected significant $P$ values (Pc) were included for discussion.

Among the MHC class I, at the HLA-A locus, frequency of HLA-A*01 allele was significantly high in controls compared to total COVID-19 cases [$X^2$value = 6.92, $Pc$ = 0.03, 95% CI, OR = 0.59(0.4–0.88)], whereas HLA-A*02 allele was significantly high in all COVID-19 cases categories (mild, severe and total) compared to controls [(Total, $X^2$ value = 27.32, $Pc < 0.001$, 95% CI, OR = 2.56 (1.79–3.67); Severe, $X^2$value = 14.17, $Pc < 0.001$, 95% CI, OR = 2.27 (1.47–3.5); and Mild, $X^2$ value = 25.02, $Pc < 0.001$, 95% CI, OR = 2.83 (1.88–4.26)]. At the HLA-B locus, frequency of HLA-B*15 was significantly high in control group compared to total COVID-19 group [$X^2$ value = 6.83, $Pc$ = 0.03, 95% CI, OR = 0.47 (0.27–0.81)], whereas HLA-B*40 allele was significantly high in mild COVID-19 cases compared to controls [Mild, $X^2$ value = 6.49, $Pc$ = 0.03, 95% CI, OR = 1.88 (1.15–3.11)]. At the HLA-C locus, HLA-Cw*01 was significantly low in severe COVID-19 cases compared to mild COVID-19 cases [$X^2$ value = 7.01, $Pc$ = 0.024, 95% CI, OR = 0.09(0.01–0.68)] (Table 1), indicating that Cw*01 association could lead to a milder course of disease. Through an ecological approach, Correale et al., had analysed whether a set of HLA A, B and C alleles known to be involved in the immune response against infections, correlates with COVID-19 incidence (Correale et al., 2020). Their data suggested susceptible role of HLA-C*01 towards SARS-CoV-2 infection and thus warranted further investigation in case-control studies. Our current data thus validated the above observation.

Among the MHC class II at the DQ-DR locus, frequencies of HLA DQB1*02 allele [Mild, $X^2$ value = 5.06, $Pc$ = 0.05, 95% CI, OR = 1.57 (1.06–2.29); Total, $X^2$ value = 5.53, $Pc$ = 0.04 with 95% CI, OR = 1.52 (1.08–2.13)], HLA DQB1*06 allele [Mild, $X^2$ value = 6.04, $Pc$ = 0.028, 95% CI, OR = 1.51 (1.1–2.1); Total, $X^2$ value = 5.84, $Pc$ = 0.04, 95% CI, OR = 1.43(1.1–1.9)] and HLA-DRB1*15 allele [Mild, $X^2$ value = 9.3, $Pc < 0.01$, 95% CI, OR = 1.67 (1.2–2.4), Total, $X^2$ value = 9.08 $Pc$ = 0.006, 95% CI, OR = 1.57 (1.2–2.1)] were significantly high in both mild COVID-19 cases and total COVID-19 cases compared to controls (Table 1). The frequency of HLA DQB1*03 was significantly high in controls compared to all patient categories [Severe, $X^2$ value = 7.13, $Pc$ = 0.02, 95% CI, OR = 0.51(0.3–0.8), Mild [$X^2$value = 11.57, $Pc$ = 0.002, 95% CI, OR = 0.49 (0.33–0.73)] and Total [$X^2$ value = 15.5, $Pc$ = 0.002, 95% CI, OR = 0.49 (0.4–0.7)] suggesting its association with reduced risk towards SARS-CoV-2 infection in consensus with Hernández-Doño

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**Table 1**
HLA Class I and II allele frequency distribution in SARS-CoV-2 infected individuals and healthy controls from Maharashtra, India.

| HLA -A Alleles | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID- 19 vs Control | | | | Severe vs Mild COVID- 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Severe 2n = 202 2n(%) | Mild 2n = 226, 2n(%) | Total 2n = 428 2n(%) | Healthy Control 2n = 450 2n(%) | $X^2$ value (p-value) | Fisher Exact p-value | OR (95% CI) | Pc-value | $X^2$ value (p-value) | Fisher Exact p- value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p- value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **A*01** | 22 (10.9) | 24 (10.6) | 46 (10.75) | 76 (16.89) | 6.92 (0.009) | **0.011** | 0.59 (0.4–0.88) | **0.03** | 3.93 (0.05) | 0.057 | 0.601 (0.36–0.99) | 0.17 | 4.207 (0.04) | 0.04 | 0.58 (0.36–0.95) | 0.12 | 0 (1) | 1 | 1.03 (0.56–1.89) | 3 |
| **A*02** | 47 (23.3) | 62 (27.4) | 109 (25.47) | 53 (11.78) | 27.32 (0.00001) | **<0.001** | 2.56 (1.79–3.67) | **<0.001** | 14.17 (0) | 0 | 2.27 (1.47–3.50) | **<0.001** | 25.02 (0.0000006) | 0.00 | 2.83 (1.88–4.26) | **<0.001** | 0.77 (0.38) | 0.37 | 0.8 (0.52–1.24) | 1.14 |
| **A*03** | 14 (6.93) | 18 (7.96) | 32 (7.48) | 22 (4.89) | 2.55 (0.11) | 0.12 | 1.57 (0.89–2.75) | 0.33 | 0.76 (0.38) | 0.35 | 1.45 (0.73–2.9) | 1.05 | 2.034 (0.15) | 0.16 | 1.68 (0.88–3.20) | 0.46 | 0.049 (0.824) | 0.72 | 0.86 (0.42–1.78) | 2.472 |
| **A*11** | 25 (12.4) | 41 (18.1) | 66 (15.42) | 69 (15.33) | 0 (1) | 1 | 1.01 (0.69–1.45) | 3 | 0.76 (0.38) | 0.34 | 0.78 (0.47–1.27) | 1.02 | 0.68 (0.41) | 0.41 | 1.22 (0.78–1.91) | 1.23 | 2.29 (0.13) | 0.109 | 0.62 (0.37–1.09) | 0.39 |
| **A*23** | 5 (2.48) | 0(0.00) | 5(1.17) | 0 (0.00) | 3.43 (0.06) | 0.03 | inf (na-inf) | 0.18 | 3.43 (0.06) | 0.03 | Inf (NA-inf) | 0.09 | NA | NA | NA | NA | 3.72 (0.054) | 0.023 | Inf (NAN-Inf) | 0.162 |
| **A*24** | 37 (18.3) | 34 (15.0) | 71 (16.59) | 61 (13.56) | 1.6 (0.21) | 0.22 | 1.27 (0.88–1.83) | 0.63 | 2.12 (0.15) | 0.124 | 1.43 (0.91–2.24) | 0.372 | 0.17 (0.68) | 0.68 | 1.13 (0.69–1.81) | 2.05 | 0.61 (0.44) | 0.37 | 1.27 (0.76–2.1) | 1.32 |
| **A*26** | 7 (3.47) | 5 (2.21) | 12 (2.80) | 13 (2.89) | 0 (1) | 1 | 0.97 (0.44–2.15) | 3 | 0.02 (0.88) | 0.81 | 1.2 (0.47–3.07) | 2.43 | 0.07 (0.79) | 0.81 | 0.76 (0.21–2.31) | 2.37 | 0.24 (0.62) | 0.56 | 1.59 (0.5–5.08) | 1.86 |
| **A*29** | 6(2.97) | 2 (0.88) | 8 (1.87) | 19 (4.22) | 4.08 (0.044) | 0.05 | 0.43 (0.19–0.99) | 0.13 | 0.3 (0.58) | 0.52 | 0.69 (0.27–1.76) | 1.56 | 4.51 (0.03) | 0.02 | 0.20 (0.02–0.85) | 0.06 | 1.52 (0.22) | 0.16 | 3.43 (0.7–17.18) | 0.66 |
| **A*30** | 3(1.49) | 3 (1.33) | 6 (1.40) | 8 (1.78) | 0.03 (0.86) | 0.79 | 0.79 (0.27–2.28) | 2.58 | 0 (1) | 1 | 0.8 (0.22–3.17) | 3 | 0.013 (0.91) | 0.94 | 0.74 (0.12–3.14) | 2.72 | 0 (1) | 1 | 1.12 (0.22–5.62) | 3 |
| **A*31** | 2(0.99) | 4 (1.77) | 6 (1.40) | 7 (1.56) | 0 (1) | 1 | 0.9 (0.3–2.69) | 3 | 0.04 (0.83) | 0.728 | 0.63 (0.13–3.07) | 2.184 | 0.013 (0.91) | 0.99 | 1.14 (0.24–4.54) | 2.72 | 0.08 (0.78) | 0.69 | 0.56 (0.10–3.06) | 2.34 |
| **A*32** | 5(2.48) | 4 (1.77) | 9 (2.10) | 19 (4.22) | 3.19 (0.074) | 0.085 | 0.49 (0.22–1.09) | 0.22 | 0.76 (0.38) | 0.37 | 0.58 (0.21–1.56) | 1.11 | 2.06 (0.15) | 0.14 | 0.41 (0.1–1.25) | 0.45 | 0.03 (0.87) | 0.74 | 1.41 (0.37–5.32) | 2.61 |
| **A*33** | 20 (9.90) | 20 (8.85) | 40 (9.35) | 65 (14.44) | 5.42 (0.02) | 0.02 | 0.61 (0.4–0.93) | 0.06 | 2.15 (0.14) | 0.13 | 0.65 (0.38–1.11) | 0.39 | 3.79 (0.05) | 0.05 | 0.56 (0.32–0.99) | 0.15 | 0.04 (0.84) | 0.74 | 1.13 (0.59–2.17) | 2.52 |
| **A*48** | 0(0.00) | 0(0.00) | 0(0.00) | 2 (0.44) | 0.45 (0.5) | 0.5 | 0 (0-nan) | 1.5 | 0.034 (0.855) | 1 | 0 (0-NaN) | 3 | NA | NA | NA | NA | NA | NA | NA | NA |
| **A*66** | 1(0.50) | 0(0.00) | 1(0.23) | 2 (0.44) | 0 (1) | 1 | 0.53 (0.05–5.81) | 3 | 0 (1) | 1 | 1.14 (0.1–12.36) | 3 | NA | NA | NA | NA | 0.003 (0.96) | 0.47 | INF (nan-inf) | 2.88 |
| **A*68** | 8(3.96) | 9(3.98) | 17 (3.97) | 34 (7.56) | 4.52 (0.034) | 0.03 | 0.51 (0.28–0.92) | 0.1 | 2.42 (0.12) | 0.087 | 0.5 (0.23–1.11) | 0.261 | 2.65 (0.10) | 0.10 | 0.51 (0.21–1.11) | 0.31 | 0 (1) | 1 | 0.99 (0.38–2.63) | 3 |

| HLA-B Allele | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID- 19 vs Control | | | | Severe vs Mild COVID- 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Severe 2n = 200 2n (%) | Mild 2n = 224, 2n (%) | Total 2n = 424 2n (%) | Healthy Control 2n = 228 2n (%) | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **B*07** | 16 (8.00) | 24 (10.7) | 40 (9.43) | 17 (7.46) | 0.5 (0.48) | 0.47 | 1.3 (0.72–2.34) | 1.44 | 0.001 (0.98) | 0.86 | 1.08 (0.53–2.2) | 2.58 | 1.086 (0.3) | 0.2973 | 1.49 (0.74–3.05) | 0.9 | 0.62(0.43) | 0.41 | 0.73 (0.37–1.41) | 1.29 |
| **B*08** | 3 (1.50) | 8 (3.57) | 11 (2.59) | 8 (3.51) | 3.94 (0.05) | 0.04 | 0.35 (0.14–0.89) | 0.15 | 1 (0.32) | 0.23 | 0.42 (0.11–1.6) | 0.69 | 0.04 (0.83) | 0.99 | 1.02 (0.32–3.18) | 2.48 | 1.06(0.3) | 0.23 | 0.41 (0.11–1.6) | 0.9 |
| **B*13** | 6 (3.00) | 8 (3.57) | 14 (3.30) | 8 (3.51) | 2.3 (0.13) | 0.105 | 0.45 (0.19–1.11) | 0.39 | 0.001 (0.98) | 0.79 | 0.85 (0.29–2.49) | 2.37 | 0.04 (0.83) | 0.99 | 1.02 (0.33–3.17) | 2.48 | 0.003 (0.96) | 0.79 | 0.84 (0.29–2.45) | 2.88 |
| **B*15** | **13 (6.50)** | **14 (6.25)** | **27 (6.37)** | **29 (12.7)** | 6.83 (0.009) | **0.008** | **0.47 (0.27–0.81)** | **0.03** | 3.98 (0.046) | 0.034 | 0.47 (0.24–0.95) | 0.102 | 4.77 (0.03) | 0.0279 | 0.46 (0.22–0.93) | 0.09 | 0(1) | 1 | 1.04 (0.48–2.28) | 3 |
| **B*18** | 2 (1.00) | 2 (0.89) | 4 (0.94) | 2 (0.88) | 0 (1) | 1 | 1.08 (0.19–5.92) | 3 | 0 (1) | 1 | 1.14 (0.16–8.18) | 3 | 0.23 (0.63) | 0.999 | 1.02 (0.07–14.2) | 1.88 | 0(1) | 1 | 1.12 (0.16–8.03) | 3 |

(*continued on next page*)

**Table 1** (*continued*)

| HLA-B Allele | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID- 19 vs Control | | | | Severe vs Mild COVID- 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Severe 2n = 200 2n (%) | Mild 2n = 224, 2n (%) | Total 2n = 424 2n (%) | Healthy Control 2n = 228 2n (%) | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **B*27** | 3 (1.50) | 0 (0.00) | 3 (0.71) | 7 (3.07) | 4.028 (0.045) | 0.038 | 0.23 (0.06–0.88) | 0.14 | 0.56 (0.45) | 0.35 | 0.48 (0.12–1.89) | 1.05 | NA (NA) | NA | NA | NA | 1.59(0.21) | 0.1 | NA (NAN-Inf)) | 0.63 |
| **B*35** | 35 (17.5) | 30 (13.4) | 65 (15.33) | 40 (17.54) | 0.39 (0.53) | 0.503 | 0.85 (0.55–1.3) | 1.59 | 0(1) | 1 | 0.99 (0.61–1.64) | 3 | 1.18 (0.28) | 0.2758 | 0.73 (0.42–1.3) | 0.83 | 1.8(0.3) | 0.28 | 1.37 (0.81–2.33) | 0.9 |
| **B*37** | 7 (3.50) | 9 (4.02) | 16 (3.77) | 3 (1.32) | 2.36 (0.13) | 0.08 | 2.94 (0.85–10.2) | 0.39 | 1.37 (0.24) | 0.2 | 2.7 (0.69–10.7) | 0.6 | 2.23 (0.14) | 0.1324 | 3.13 (0.76–18.2) | 0.41 | 0.001 (0.98) | 0.81 | 0.87 (0.32–2.37) | 2.94 |
| **B*38** | 4 (2.00) | 0 (0.00) | 4 (0.94) | 2 (0.88) | 0(1) | 1 | 1.08 (0.19–5.92) | 3 | 0.33 (0.57) | 0.43 | 2.3 (0.42–12.7) | 1.29 | NA (NA) | NA | NA | NA | 2.6(0.104) | 0.05 | INF (NAN-Inf)) | 0.312 |
| **B*39** | 2 (1.00) | 0 (0.00) | 2 (0.47) | 0 (0) | 0.088 (0.77) | 0.54 | Inf (NAN-Inf) | 2.31 | 0.65 (0.42) | 0.22 | Inf (NAN-Inf) | 0.66 | NA | NA | NA | NA | 0.63(0.43) | 0.2 | INF (NAN-Inf)) | 1.29 |
| **B*40** | 37 (18.5) | 57 (25.5) | 94 (22.17) | 35 (15.35) | 3.93 (0.048) | 0.039 | 1.57 (1.03–2.4) | 0.14 | 0.55 (0.46) | 0.44 | 1.3 (0.75–2.08) | 1.32 | 6.49 (0.01) | 0.0106 | 1.88 (1.15–3.11) | 0.03 | 2.57(0.11) | 0.1 | 0.67 (0.42–1.1) | 0.33 |
| **B*41** | 1 (0.50) | 0 (0.00) | 1 (0.24) | 0 (0) | 0(1) | 1 | Inf (NAN-Inf) | 3 | 0.004 (0.948) | 0.47 | Inf (NAN-Inf) | 1.41 | NA | NA | NA | NA | 0.003 (0.955) | 0.47 | INF (NAN-Inf)) | 2.865 |
| **B*44** | 18 (9.00) | 11 (4.91) | 29 (6.84) | 18 (7.89) | 0.114 (0.74) | 0.64 | 0.86 (0.47–1.58) | 2.22 | 0.06 (0.8) | 0.73 | 1.15 0.58–2.28 | 2.19 | 1.22 (0.27) | 0.27 | 0.6 (0.27–1.31) | 0.81 | 2.2(0.14) | 0.123 | 1.92 (0.88–4.16) | 0.42 |
| **B*47** | 2 (1.00) | 0 (0.00) | 2 (0.47) | 0 (0) | 0.088 (0.77) | 0.54 | Inf (NAN-Inf) | 2.31 | 0.65 (0.42) | 0.22 | Inf (NAN-Inf) | 0.66 | NA | NA | NA | NA | 0.63(0.43) | 0.22 | NA (NAN-Inf)) | 1.29 |
| **B*49** | 5 (2.50) | 0 (0.00) | 5 (1.18) | 2 (0.88) | 0 (1) | 1 | 1.35 0.26–7.01 | 3 | 0.88 (0.35) | 0.26 | 2.89 0.56–15.1 | 0.78 | NA | NA | NA | NA | 3.73 (0.054) | 0.023 | NA (NAN-Inf)) | 0.162 |
| **B*50** | 1 (0.50) | 1 (0.45) | 2 (0.47) | 0 (0) | 0.088 (0.77) | 0.54 | Inf (NAN-Inf) | 2.31 | 0.004 (0.95) | 0.47 | Inf (NAN-Inf) | 1.41 | NA | NA | NA | NA | 0(1) | 1 | 1.12 (0.1–18.03) | 3 |
| **B*51** | 16 (8.00) | 23 (10.27) | 39 (9.20) | 19 (8.33) | 0.051 (0.821) | 0.774 | 1.114 (0.63–1.95) | 2.46 | 0(1) | 1 | 0.96 (0.48–1.92) | 3 | 0.29 (0.58) | 0.5851 | 1.26 (0.64–2.52) | 1.75 | 0.41(0.52) | 0.5 | 0.76 (0.39–1.48) | 1.56 |
| **B*52** | 17 (8.50) | 13(5.80) | 30 (7.08) | 16 (7.02) | 0 (1) | 1 | 1.01 (0.54–1.89) | 3 | 0.15 (0.695) | 0.59 | 1.23 (0.61–2.51) | 1.77 | 0.11 (0.74) | 0.7388 | 0.82 (0.35–1.86) | 2.21 | 0.79(0.37) | 0.34 | 1.51 (0.7–3.19) | 1.11 |
| **B*53** | 1 (0.50) | 1 (0.45) | 2 (0.47) | 1 (0.44) | 0 (1) | 1 | 1.08 (0.09–11.9) | 3 | 0 (1) | 1 | 1.14 (0.7–18.4) | 3 | 0.48 (0.49) | 0.9999 | 1.02 (0.01–80.3) | 1.46 | 0(1) | 1 | 1.12 (0.1–18.03) | 3 |
| **B*55** | 1 (0.50) | 2 (0.89) | 3 (0.71) | 5 (2.19) | 1.6 (0.2) | 0.136 | 0.32 (0.08–1.34) | 0.6 | 1.15 (0.28) | 0.22 | 0.22 (0.03–1.94) | 0.66 | 0.55 (0.46) | 0.4641 | 0.4 (0.08–2.1) | 1.38 | 0(1) | 1 | 0.56 (0.05–6.2) | 3 |
| **B*56** | 0 (0.00) | 4(1.79) | 4 (0.94) | 2 (0.88) | 0 (1) | 1 | 1.08 (0.19–5.92) | 3 | 0.38 (0.54) | 0.5 | Inf (NAN-Inf) | 1.5 | 0.18 (0.67) | 0.6688 | 2.06 (0.4–11.3) | 2 | 1.95(0.16) | 0.13 | 0 (0-NaN) | 0.48 |
| **B*57** | 4 (2.00) | 7 (3.13) | 11 (2.59) | 7 (3.07) | 0.01 (0.92) | 0.8 | 0.84 (0.32–2.2) | 2.76 | 0.15 (0.69) | 0.55 | 0.64 (0.19–2.23) | 1.65 | 0.056 (0.81) | 0.999 | 1.01 (0.6–1.72) | 2.44 | 0.18(0.67) | 0.56 | 0.63 (0.18–2.19) | 2.01 |
| **B*58** | 6 (3.00) | 10 (4.46) | 16 (3.77) | 7 (3.07) | 0.06 (0.81) | 0.82 | 1.24 (0.5–3.06) | 2.43 | 0(1) | 1 | 0.98 (0.32–2.96) | 3 | 0.28 (0.6) | 0.596 | 1.48 (0.55–3.95) | 1.79 | 0.29(0.59) | 0.46 | 0.67 (0.24–1.86) | 1.77 |

| HLA-C Alleles | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID-19 vs Control | | | | Severe vs Mild COVID-19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Severe 2n = 202 2n(%) | Mild 2n = 226, 2n(%) | Total 2n = 428 2n(%) | Control 2n = 222 2n(%) | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **C*01** | 1 (0.5) | 12 (5.31) | 13 (3.30) | 9 (4.05) | 0.05 (0.82) | 0.66 | 0.82 (0.35–1.95) | 2.46 | 4.4 (0.036) | 0.021 | 0.12 (0.02–0.94) | 0.063 | 0.16 (0.69) | 0.69 | 1.33 (0.54–3.22) | 2.07 | 7.01 (0.008) | **0.004** | **0.09 (0.01–0.68)** | **0.024** |
| **C*02** | 2 (0.99) | 2 (0.88) | 4 (1.02) | 1 (0.45) | 0.08 (0.78) | 0.659 | 2.27 (0.25–20.4) | 2.34 | 0.007 (0.94) | 0.61 | 2.21 (0.19–24.56) | 1.83 | 0.0002 (0.99) | 0.99 | 1.97 (0.12–116.9) | 2.96 | 0 (1) | 1 | 1.1 (0.15–8.02) | 3 |
| **C*03** | 10 (4.95) | 17 (7.52) | 27 (6.85) | 21 (9.46) | 1 (0.16) | 0.32 | 0.70 (0.39–1.28) | 0.33 | 2.5 (0.11) | 0.093 | 0.5 (0.23–1.09) | 0.279 | 0.3207 (0.57) | 0.57 | 0.78 (0.37–1.6) | 1.71 | 0.79 (0.37) | 0.32 | 0.64 (0.29–1.43) | 0.4 |

(*continued on next page*)

**Table 1** (*continued*)

| HLA-C Alleles | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID-19 vs Control | | | | Severe vs Mild COVID-19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Severe 2n = 202 2n(%) | Mild 2n = 226, 2n(%) | Total 2n = 428 2n(%) | Control 2n = 222 2n(%) | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **C*04** | 34 (16.83) | 36 (15.93) | 70 (17.77) | 42 (18.92) | 0.06 (0.81) | 0.75 | 0.93 (0.61–1.4) | 2.43 | 0.19 (0.67) | 0.61 | 0.87 (0.53–1.43) | 1.83 | 0.50 (0.48) | 0.48 | 0.81 (0.48–1.36) | 1.43 | 0.02 (0.9) | 0.89 | 1.07 (0.64–1.78) | 2.7 |
| **C*05** | 1 (0.5) | 1 (0.44) | 2(0.51) | 0 (0) | 0.11 (0.75) | 0.54 | Inf (Nan-Inf) | 2.25 | 0.003 (0.96) | 0.47 | Inf (Nan-Inf) | 1.41 | NA | NA | NA | NA | 0 (1) | 1 | 1.12 (0.1–18.01) | 3 |
| **C*06** | 19 (9.41) | 18 (7.96) | 37 (9.39) | 14 (6.31) | 1.4 (0.24) | 0.22 | 1.54 (0.81–2.92) | 0.72 | 1.08 (0.3) | 0.3 | 1.6 (0.76–3.2) | 0.9 | 0.25 (0.62) | 0.62 | 1.29 (0.62–2.65) | 1.86 | 0.13 (0.72) | 0.61 | 1.2 (0.61–2.36) | 2.16 |
| **C*07** | 53 (26.24) | 49 (21.68) | 102 (25.89) | 44 (19.82) | 2.57 (0.11) | 0.09 | 1.41 (0.95–2.1) | 0.33 | 2.29 (0.13) | 0.11 | 1.46 (0.93–2.3) | 0.33 | 0.14 (0.71) | 0.71 | 1.12 (0.69–1.82) | 2.14 | 0.98 (0.32) | 0.31 | 1.29 (0.82–2.01) | 0.96 |
| **C*08** | 1 (0.5) | 3 (1.33) | 4 (1.02) | 5 (2.25) | 0.77 (0.38) | 0.29 | 0.45 (0.12–1.68) | 1.14 | 1.22 (0.27) | 0.22 | 0.22 (0.03–1.88) | 0.66 | 0.15 (0.7) | 0.7 | 0.58 (0.089–3.05) | 2.11 | 0.15 (0.69) | 0.63 | 0.37 (0.04–3.58) | 2.07 |
| **C*12** | 39 (19.31) | 31 (13.72) | 70 (17.77) | 33 (14.86) | 0.66 (0.42) | 0.37 | 1.24 (0.79–1.94) | 1.26 | 1.18 (0.28) | 0.25 | 1.4 (0.82–2.28) | 0.75 | 0.05 (0.83) | 0.83 | 0.91 (0.54–1.55) | 2.5 | 2.05 (0.15) | 0.15 | 1.51 (0.89–2.52) | 0.45 |
| **C*14** | 9 (4.46) | 11 (4.87) | 20 (5.08) | 8 (3.60) | 0.41 (0.52) | 0.55 | 1.43 (0.62–3.3) | 1.56 | 0.05 (0.83) | 0.81 | 1.26 (0.48–3.33) | 2.43 | 0.18 (0.67) | 0.67 | 1.37 (0.49–3.99) | 2 | 0 (1) | 1 | 0.91 (0.37–2.25) | 3 |
| **C*15** | 27 (13.37) | 40 (17.7) | 67 (17.01) | 36 (16.22) | 0.02 (0.89) | 0.82 | 1.01 (0.68–1.65) | 2.67 | 0.42 (0.52) | 0.49 | 0.81 (0.47–1.38) | 1.47 | 0.085 (0.77) | 0.77 | 1.11 (0.66–1.88) | 2.31 | 1.2 (0.27) | 0.23 | 0.72 (0.42–1.22) | 0.81 |
| **C*16** | 5 (2.48) | 6 (2.65) | 11 (2.79) | 8 (3.60) | 0.1 (0.75) | 0.63 | 0.77 (0.3–1.94) | 2.25 | 0.14 (0.71) | 0.58 | 0.69 (0.22–2.13) | 1.74 | 0.09 (0.76) | 0.76 | 0.73 (0.21–2.45) | 2.28 | 0 (1) | 1 | 0.93 (0.28–3.09) | 3 |
| **C*17** | 1 (0.5) | 0 (0) | 1 (0.25) | 1 (0.45) | 0 (1) | 1 | 0.56 (0.04–9.04) | 3 | 0(1) | 1 | 1.11 (0.07–17.87) | 3 | NA | NA | NA | NA | 0.003 (0.96) | 0.47 | INF NAN-INF | 2.88 |
| **C*18** | 0 (0) | 0 (0) | 0 (0) | 1 (0.45) | 0.09 (0.77) | 0.36 | NA | 2.31 | 0(1) | 1 | 0 (0-NaN) | 3 | NA | NA | NA | NA | NA | NA | NA | NA |

| HLA-ABC-Alleles | Sever 2n = 200 2n(%) | Mild 2n = 224, 2n(%) | Total 2n = 432 2n(%) | Control 2n = 220 2n(%) | Total COVID-19 vs Control | | | Severe COVID-19 vs Control | | | Mild COVID-19 vs Control | | | Sever vs Mild COVID-19 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **A*02:B*:35:C*04** | 11 (5.53) | 1 (0.523) | 22 (3.5) | 6 (2.56) | 0.183 (0.67) | 0.67 | 1.35 (0.54–3.37) | 2.01 | 1.42 (0.23) | 0.22 | 2.07 (0.75–5.7) | 0.69 | 2.39 (0.12) | 0.06 | 0.16 (0.02–1.34) | 0.36 | **7.96 (0.005)** | **0.002** | **12.9 (1.6–100.4)** | **0.02** |

| HLA-DQ Alleles | COVID-19 | | | Control | Total COVID-19 Vs Control | | | | Sever COVID-19 Vs Control | | | | Mild COVID-19 Vs Control | | | | Sever vs Mild Covid- 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sever 2n = 164 2n(%) | Mild 2n = 268 2n(%) | Total 2n = 432 2n(%) | Controls 2n = 440 2n(%) | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value | $X^2$ value (p-value) | Fisher Exact p-value | OR 95% CI | Pc-value |
| **DQB1*2** | 36 (21.95) | 63 (23.51) | 99 (22.92) | 16.36 | 5.53 (0.019) | 0.02 | 1.52 (1.08–2.13) | **0.04** | 2.17 (0.14) | 0.12 | 1.44 (0.92–2.25) | 0.28 | 5.06 (0.025) | **0.023** | 1.57 (1.06–2.29) | **0.05** | 0.07 (0.79) | 0.725 | 0.92 (0.57–1.46) | 1.58 |
| **DQB1*3** | 24 (14.63) | 38 (14.18) | 62 (14.35) | 111 (25.23) | 15.5 (<0.0001) | <0.001 | 0.49 (0.35–0.70) | **0.002** | 7.13 (0.008) | 0.008 | 0.508 (0.313–0.824) | **0.02** | 11.57 (0.001) | 0.001 | 0.49 (0.33–0.73) | **0.002** | 0.00 (1) | 0.89 | 1.04 (0.59–1.80) | 2 |
| **DQB1*4** | 0 (0) | 4 (1.49) | 4 (0.93) | 7 (1.59) | 0.33 (0.56) | 1 | 0.58 (0.17–1.99) | 1.12 | 1.43 (0.23) | 0.198 | 0 (0-NaN) | 0.39 | 0.0 (1) | 1 | 0.94 (0.27–3.2) | 2 | 1.11 (0.29) | 0.3 | 0 (0-NaN) | 0.58 |
| **DQB1*5** | 46 (28.05) | 59 (22.01) | 105 (24.31) | 120 (27.27) | 0.85 (0.36) | 0 | 0.86 (0.63–1.16) | 0.72 | 0.008 (0.93) | 0.84 | 1.04 (0.69–1.55) | 1.86 | 2.17 (0.14) | 0.13 | 0.75 (0.53–1.08) | 0.282 | 1.6 (0.19) | 1.67 | 1.38 (0.88–2.2) | 0.38 |
| **DQB1*6** | 58 (35.37) | 104 (38.81) | 162 (37.50) | 130 (29.55) | 5.84 (0.016) | 0.02 | 1.43 (1.08–1.89) | **0.04** | 1.63 (0.2) | 0.2 | 1.3 (0.89–1.91) | 0.4 | 6.04 (0.014) | 0.013 | 1.51 (1.09–2.08) | **0.028** | 0.38 (0.54) | 0.54 | 0.86 (0.58–1.29) | 1.08 |

| Alleles | COVID-19 | | | Control | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID-19 vs Control | | | | Sever vs Mild COVID-19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HLA-DR Alleles | Sever 2n = 164 2n(%) | Mild 2n = 268, 2n(%) | Total 2n = 432 2n(%) | Control 2n = 456 2n(%) | *$X^2$ value (p-value)* | *Fisher Exact p-value* | OR 95% CI | *Pc-value* | *$X^2$ value (p-value)* | *Fisher Exact p-value* | OR 95% CI | *Pc-value* | *$X^2$ value (p-value)* | *Fisher Exact p-value* | OR 95% CI | *Pc-value* | *$X^2$ value (p-value)* | *Fisher Exact p-value* | OR 95% CI | *Pc-value* |
| **DRB1*01** | 7 (4.27) | 10 (3.73) | 17 (4) | 14 (3.07) | 0.27 (0.60) | 0.58 | 1.29 (0.63–2.66) | 1.2 | 0.23 (0.63) | 0.46 | 1.41 (0.56–3.56) | 1.962 | 0.07 (0.79) | 0.67 | 1.22 (0.54–2.79) | 1.58 | 0.001 (0.98) | 0.8 | 1.15 (0.43–3.08) | 1.962 |
| **DRB1*03** | 12 (7.32) | 17 (6.34) | 29 (7) | 32 (7.02) | 0.002 (0.96) | 0.89 | 0.95 (0.56–1.60) | 1.92 | 0.00(1) | 0.86 | 1.17 (0.54–2.51) | 1.7 | 0.04 (0.85) | 0.76 | 0.89 (0.48–1.65) | 1.7 | 0.04 (0.69) | 0.85 | 1.17 (0.54–2.51) | 1.7 |
| **DRB1*04** | 16 (9.76) | 17 (6.34) | 33 (8) | 43 (9.43) | 0.69 (0.41) | 0.4 | 0.79 (0.49–1.28) | 0.82 | 0.00 (1) | 0.88 | 1.04 (0.57–1.89) | 2 | 1.73 (0.18) | 0.16 | 0.65 (0.36–1.16) | 0.36 | 1.2 (0.27) | 0.19 | 1.59 (0.78–3.25) | 0.38 |
| **DRB1*07** | 23 (14.02) | 36 (13.43) | 59 (14) | 62 (13.6) | 0.00 (1) | 1 | 1 (0.69–1.48) | 2 | 0.0 (0.99) | 0.89 | 1.04 (0.62–1.74) | 1.954 | 0.00 (1) | 1 | 0.98 (0.61–1.56) | 2 | 0.001 (0.98) | 0.89 | 1.05 (0.59–1.85) | 1.78 |
| **DRB1*08** | 1 (0.61) | 2 (0.75) | 3 (1) | 8 (1.75) | 1.26 (0.26) | 0.23 | 0.39 (0.10–1.49) | 0.46 | 0.45 (0.5) | 0.46 | 0.34 (0.04–2.76) | 0.92 | 0.63 (0.43) | 0.34 | 0.42 (0.08–1.99) | 0.86 | 0.00(1) | 1 | 0.82 (0.073–9.07) | 2 |
| **DRB1*09** | 0 (0) | 1 (0.37) | 1 (0) | 10 (2.19) | 5.47 (0.019) | 0.012 | 0.10 (0.01–0.81) | **0.038** | 2.4 (0.121) | 0.07 | 0 (0-NaN) | 2 | 2.62 (0.1) | 0.06 | 0.16 (0.02–1.31) | 0.2 | 0.00(1) | 1 | 0 (0-NaN) | 2 |
| **DRB1*10** | 11 (6.71) | 13 (4.85) | 24 (6) | 42 (9.21) | 3.79 (0.05) | 0.041 | 0.58 (0.35–0.98) | 0.1 | 0.67 (0.41) | 0.42 | 0.71 (0.36–1.41) | 0.82 | 3.97 (0.05) | 0.04 | 0.50 (0.26–0.95) | 0.1 | 0.36 (0.55) | 0.52 | 1.41 (0.62–3.23) | 1.1 |
| **DRB1*11** | **9 (5.49)** | **11 (4.1)** | **20 (5)** | **44 (9.65)** | 7.6 (0.006) | 0.004 | 0.46 (0.26–0.78) | **0.012** | 2.12 (0.14) | 0.141 | 0.54 (0.26–1.14) | 1.34 | 6.62 (0.01) | 0.006 | 0.38 (0.19–0.76) | **0.02** | 0.18 (0.66) | 0.49 | 1.36 (0.5–3.35) | 1.32 |
| **DRB1*12** | 1 (0.61 | 4 (1.49) | 5 (1) | 5 (1.1) | 0.00 (1) | 1 | 1.06 (0.3–3.67) | 2 | 0.007 (0.94) | 1 | 0.55 (0.06–4.77) | 1.88 | 0.014 (0.91) | 0.73 | 1.36 (0.27–6.41) | 1.82 | 0.14 (0.71) | 0.65 | 0.4 (0.05–3.63) | 1.42 |
| **DRB1*13** | 14 (8.54) | 22 (8.21) | 36 (8) | 30 (6.58) | 0.75 (0.39) | 0.37 | 1.29 (0.78–2.13) | 0.78 | 0.43 (0.51) | 0.38 | 1.33 (0.68–2.57) | 1.02 | 0.45 (0.5) | 0.5 | 1.27 (0.68–2.33) | 1 | 0.00(1) | 1 | 1.04 (0.52–2.1) | 2 |
| **DRB1*14** | 15 (9.15) | 34 (12.69) | 49 (11) | 42 (9.21) | 0.87 (0.35) | 0.32 | 1.26 (0.82–1.95) | 0.7 | 0.0(1) | 1 | 0.99 (0.53–1.84) | 2 | 1.82 (0.18) | 0.17 | 1.43 (0.86–2.38) | 0.36 | 0.94 (0.33) | 0.28 | 0.69 (0.37–1.32) | 0.66 |
| **DRB1*15** | **54 (32.93)** | **99 (36.94)** | **153 (35)** | **118 (25.88)** | 9.08 (0.003) | 0.002 | 1.57 (1.18–2.09) | **0.006** | 2.65 (0.10) | 0.09 | 1.41 (0.95–2.07) | 0.2 | 9.3 (0.002) | 0.002 | 1.67 (1.19–2.35) | **<0.01** | 0.55 (0.46) | 0.41 | 0.84 (0.56–1.26) | 0.92 |
| **DRB1*16** | 1 (0.61) | 2 (0.75) | 3 (0.6) | 6 (1.32) | 0.35 (0.56) | 0.51 | 0.52 (0.13–2.1) | 1.12 | 0.09 (00.76) | 0.68 | 0.46 (0.05–3.85) | 1.36 | 0.12 (0.73) | 2.72 | 0.56 (0.11–2.8) | 1.5 | 0.00 (1) | 1 | 0.82 (0.07–9.1) | 2 |

| HLA-DR Alleles | Sever 2n = 164 2n(%) | Mild 2n = 268, 2n(%) | Total 2n = 432 2n(%) | Control 2n = 386 2n(%) | Total COVID-19 vs Control | | | | Severe COVID-19 vs Control | | | | Mild COVID-19 vs Control | | | | Sever vs Mild COVID-19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **DQB1*06:DRB1*15** | 43 (26.22) | 81 (30.07) | 124 (28.70) | 84 (21.8) | 4.82 (0.03) | 0.03 | 1.45 (1.05–1.99) | 0.06 | 1.05 (0.31) | 0.27 | 1.28 (0.84–1.95) | 0.54 | 5.56 (0.02) | **0.02** | **1.56 (1.09–2.22)** | **0.04** | 0.61 (0.43) | 0.4 | 0.82 (0.5–1.3) | 0.8 |

et al., 2022. It is interesting to note that the allele frequencies of both HLA-DRB1*09 [$X^2$ value = 5.47, *Pc* = 0.04, 95% CI, OR = 0.10 (0.01–0.81)] and HLA-DRB1*11 [$X^2$ value = 7.6, *Pc* = 0.01, 95% CI, OR = 0.46 (0.3–0.8)] were significantly high in the COVID-19 negative healthy controls compared to total COVID-19 cases rendering them as protective alleles (Table 1). Haplotype frequencies of ≥5% in either groups were only considered. HLA A*02-B*35-C*04 haplotype may be significant in severe COVID-19 compared to mild COVID-19. The larger spread in the width of the CI may be attributed to the variability in the data [$X^2$ value = 7.96, *Pc* = 0.02, with 95% CI and OR = 12.9 (1.6–101.5)]. DQB1*06-DRB1*15 haplotype frequency was significantly high in mild COVID-19 cases compared to controls [Mild, $X^2$ value = 5.56, *Pc* = 0.04, 95% CI, OR = 1.56 (1.09–2.22)].

Tomita et al., assessed the global distribution of HLA genes and examined the association of the most frequent HLA alleles with prevalence and mortality of COVID-19. Further *in-silico* binding prediction of HLA class I alleles for SARS-CoV-2 indicated HLA-A*02:01 to have a relatively lower capacity to present SARS-CoV-2 antigens and thus associated it with an increased risk for COVID-19 (Tomita et al., 2020). In a similar line, we show an association between HLA-A*02 and susceptibility to COVID-19. It could be suggested that individuals with HLA-A*02 may have a lower capacity to present SARS-CoV-2 antigens and thus may generate a truncated T-cell-mediated antiviral responses to SARS-CoV-2.

A report by Abdelhafiz et al., provided interesting insights into the association between HLA class I (HLA-B*15) allele and protection from COVID-19 disease / severity of COVID-19 through immune response modulation in Egyptian patients (Abdelhafiz et al., 2022). *In-silico*/ Computational data analysis of viral peptide-MHC class I binding affinity across HLA-A, -B, and-C genotypes for all SAR S-CoV-2 peptides by Nguyen et al., suggested that HLA-B*15:03 allele have the highest binding affinity for viral peptides and hence could act as a protective allele (Migliorini et al., 2021; Nguyen et al., 2020). Lower allele frequencies of HLA-B*15 in the patient population of the current study suggested its association with reduced risk towards SARS-CoV-2 infection. The current study on COVID-19 patients elucidating higher HLA-DRB1*11 allele in control group goes hand in hand with our previous reports on distribution of HLA class II alleles in chikungunya and hepatitis E patients indicating HLA DRB1*11 as a resistant allele against both CHIKV and HEV infections (Thanapati et al., 2014; Das et al., 2013). Therefore, it may be possible that the epitopes presented by HLA-DRB1* 11 perhaps induce protective immune response in Indian patients with viral etiology, however, in depth studies are needed to understand the associated mechanism. Similar to our data, higher frequencies of DRB1*15 and DQB1*06 in 99 severely affected COVID-19 Italian patients and in Mexican population could be indicative of the same as global susceptible alleles for COVID-19 infection (Hernández-Doño et al., 2022; Novelli et al., 2020) (Table 1). Association of HLA-DRB1*11 as a protective, DRB1*15 and DQB1*06 as susceptible alleles and the emergence of DQB1*06-DRB1*15 haplotype as susceptible haplotypes towards COVID-19 infection is being reported for the first time in our population similar to that reported in Mexican population suggesting that genetic susceptibility and/or resistance to COVID-19 infection may be modulated by HLA class II alleles (Hernández-Doño et al., 2022). Recently, in ChAdOx1 nCov-19 vaccine efficacy trials in 1076 participants in the United Kingdom, an association of higher levels of anti-RBD antibody response with HLA-DQB1*06 allele was detected. The study observed that individuals carrying HLA-DQB1*06 allele were less likely to experience breakthrough infection. Overall, the study demonstrated an association of HLA allele with COVID-19 vaccine antibody response and risk of breakthrough infection, with implications for future vaccine design and implementation. (Mentzer et al., 2023). In a similar line, CoVac-1(composed of SARS-CoV-2 HLA-DR T cell epitopes derived from various viral proteins combined with the Toll-like receptor 1/2 agonist XS15), a vaccine candidate currently ongoing phase II clinical trial, was developed with the objective to induce strong SARS-CoV-2 T cell immunity against COVID-19. The IFN-γ T cell responses induced by CoVac-1 persisted and were higher compared to those detected after SARS-CoV-2 infection/vaccination with other approved vaccines, hereby establishing the evidence that inclusion of certain HLA restricted epitopes in a vaccine enhances T cell immunity and thus may influence future vaccination strategies (Heitmann et al., 2022).

Overall, the current study suggests that identifying the HLA alleles associated with the severity of COVID-19/susceptibility to SARS-CoV-2 infection may help identify the vulnerable population and may also provide support towards future vaccination strategies.

## Ethical statements

The study was approved by the Institutional Ethical Committee for Research on Humans, based on the guidelines set by the Indian Council of Medical Research, New Delhi. Informed written consent was obtained from all study participants.

## Authorship contribution statement

Conceptualization: A.S.T; Methodology: PW, SV, KA, AST, Software: PW, SV, Resources: SPT, PJ, AK, MB,YG, NK, LN, Writing original draft preparation: A.S.T, PW, Funding acquisition: A.S.T, PA. All authors have read and agreed to the final version of the manuscript.

## Declaration of Competing Interest

Authors do not have any conflict of interest.

## Data availability

Data will be made available on request.

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