The association of human leucocyte antigen (HLA) alleles with COVID-19 severity: A systematic review and meta-analysis

Abstract

Due to their pivotal role in orchestrating the immune response, HLA loci were recognized as candidates for genetic association studies related to the severity of COVID-19. Since the findings on the effects of HLA alleles on the outcome of SARS-CoV-2 infection remain inconclusive, we aimed to elucidate the potential involvement of genetic variability within HLA loci in the molecular genetics of COVID-19 by classifying the articles according to different disease severity/outcomes and by conducting a systematic review with meta-analysis. Potentially eligible studies were identified by searching PubMed, Scopus and Web of Science literature databases. A total of 28 studies with 13,073 participants were included in qualitative synthesis, while the results of 19 studies with 10,551 SARS-CoV-2-positive participants were pooled in the meta-analysis. According to the results of quantitative data synthesis, association with COVID-19 severity or with the lethal outcome was determined for the following alleles and allele families: HLA-A*01, HLA-A*03, HLA-A*11, HLA-A*23, HLA-A*31, HLA-A*68, HLA-A*68:02, HLA-B*07:02, HLA-B*14, HLA-B*15, HLA-B*40:02, HLA-B*51:01, HLA-B*53, HLA-B*54, HLA-B*54:01, HLA-C*04, HLA-C*04:01, HLA-C*06, HLA-C*07:02, HLA-DRB1*11, HLA-DRB1*15, HLA-DQB1*03 and HLA-DQB1*06 (assuming either allelic or dominant genetic model). We conclude that alleles of HLA-A, -B, -C, -DRB1 and -DQB1 loci may represent potential biomarkers of COVID-19 severity and/or mortality, which needs to be confirmed in a larger set of studies.