Association of ACE2 and TMPRSS2 genetic variants with COVID-19 severity in the Malaysian population

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ABSTRACT

Introduction: Genetic variation among populations influences infection severity, with specific genetic differences shaping individual responses to viral infection. Variants in angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) play crucial roles in viral entry, modulating infections, and impacting disease progression, particularly in COVID-19. This study aims to determine the association between specific genetic variants in Malaysians COVID-19 patients and disease severity. **Materials and Methods:** This study identified two SNPs (rs2285666 and rs4240157) in ACE2 and one SNP (rs2070788) in TMPRSS2 in COVID-19 patients' blood samples collected at Hospital Sungai Buloh using conventional allele-specific polymerase chain reaction (ASPCR). Human DNA was extracted from 110 clinical blood samples and amplified using pre-designed primer sequences. The selected bands were further validated using Sanger sequencing. Genotypes were compared between non-severe (53 patients) and severe (57 patients) groups. **Results:** Our major findings indicate an association between the TMPRSS2 (rs2070788) G allele and an increased likelihood of developing severe COVID-19 (RR 5.65, OR 6.14, 95% CI:1.32-28.57, $p < .05$). However, no significant association was observed between ACE2 variants (rs2285666 and rs4240157) and COVID-19 severity. **Conclusion:** The data suggest that the G allele at rs2070788 of the TMPRSS2 gene plays a significant role in determining the severity of COVID-19. Further studies with larger cohorts are warranted to provide stronger evidence and enhance our understanding of the genetic factors influencing COVID-19 severity.