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Association between metabolic-associated fatty liver disease and Covid-19 severity: A genetic analysis

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Background. This study aimed to link specific single nucleotide polymorphisms (SNPs) in the IFNAR2 rs2236757, ACE2 rs2074192, OAS1 rs10774671 and OAS3 rs10735079 genes to COVID-19 severity in MAFLD (metabolic-associated fatty liver disease) patients. These genes influence interferon, antiviral responses, and viral entry. **Methods.** A single-center prospective cohort study included COVID-19 patients with/without MAFLD and a control group. The data on demographics, medical history, clinical features, lab results, and genetic analysis were collected. Genetic analysis was conducted to determine the potential associations between specific gene variations and COVID-19 severity. **Results.** Unlike the previous findings on the IFNAR2 rs2236757, we found no link to COVID-19 severity. The rs2236757 A allele was associated with significantly higher creatinine levels upon hospital admission (88.5 mmol/L vs. 50 mmol/L, p = 0.021) compared to individuals without the A allele. In contrast, the rs2236757 G allele demonstrated a negative correlation with neutrophil levels in the discharged patients (r = –0.30, p = 0.012). No association was found between the rs2236757 polymorphism and MAFLD. Our study on Ukrainian population's genotype and allele distribution for OAS1 rs10774671 and OAS3 rs10735079 were similar to those in the European reference population. These SNPs were not associated with COVID-19 severity. However, the OAS3 rs10735079 G allele was associated with significantly higher monocyte levels (r = 0.23, p = 0.048), hematocrit (r = 0.27, p = 0.023), and total protein levels (r = 0.29, p = 0.015) compared to the non-G allele. Furthermore, the homozygous GG genotype demonstrated a similar positive correlation with hematocrit (r = 0.28, p = 0.019) and total protein levels (r = 0.26, p = 0.025). While the OAS1 rs10774671 G allele howed a trend towards association with COVID-19 severity (p=0.052), it was not statistically significant. Neither SNP was linked to MAFLD. Our study on the population's ACE2 rs2074192 genotype and allele distribution differed from the European reference. This SNP was not associated with COVID-19 severity or MAFLD. However, the ACE2 rs2074192 C allele carriers exhibited significantly lower band neutrophil levels compared to non-carriers (3 mmol/L vs 9 mmol/L, IQR: 2–7 mmol/L vs. IQR: 6–13.5, p = 0.046). Conversely, the individuals with the C allele presented with higher total bilirubin levels compared to those without the C allele (12.4 mmol/L vs. 21.9 mmol/L, IQR: 10.8–14.9 mmol/L vs. IQR: 20.5–107 mmol/L; p = 0.004). **Conclusions.** This study did not find an association between the genetic parameters investigated and severity of COVID-19 disease in patients with MAFLD. Our findings emphasize the need for further research considering population differences and additional genetic and environmental variables. **Grants.** This research received financial support from RECOOP Grant #36—CSMC Senior Scientists (RCSS) "Comprehensive Analysis of Genetic Predictors for MAFLD Development in Patients with COVID-19". **Ethical Committee Approval.** Ethical Committee Approval from I. Horbachevsky Ternopil National Medical University, Protocol No. 75, dated 1 November 2023.

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