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ACE2 POLYMORPHISM: THE HUMAN KEY FOR COVID-19 SEVERITY

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ABSTRACT

COVID-19, caused by the novel coronavirus SARS-CoV-2, has rapidly evolved into a global pandemic, profoundly impacting public health, economies, and societies worldwide. The disease's variable clinical manifestations range from asymptomatic cases to severe respiratory distress, highlighting the critical need to understand the genetic underpinnings of COVID-19 susceptibility and severity. This study aims to investigate the association between *ACE2* gene polymorphisms and COVID-19 susceptibility and severity, providing insights that could be pivotal for developing targeted preventive and therapeutic strategies. ACE2, a transmembrane protein, is recognized as the primary entry point for SARS-CoV-2 into host cells. It is expressed in various tissues, including the lungs, heart, kidneys, and intestines, suggesting its central role in the multi-organ impact of the virus. Genetic variations in the *ACE2* gene have been implicated in influencing an individual's susceptibility to and severity of COVID-19. Such variations can affect *ACE2* expression levels or alter the protein's structure, potentially influencing the virus's ability to bind and enter cells. To elucidate these associations, we conducted a comprehensive genome mining analysis of 203 genomes from individuals diagnosed with COVID-19. Our analysis focused on identifying *ACE2* polymorphisms associated with the disease. We analyzed a comprehensive set of 22 genetic markers across 15 genes linked to COVID-19 susceptibility from existing literature. These markers were chosen based on their documented association with immune response, viral entry mechanisms, and inflammatory processes in viral infections. Individuals were stratified into one of seven risk categories based on their genetic profiles: “Moderately increased infection risk”, “Moderately reduced infection risk”, “Roughly average infection risk”, “Slightly increased infection risk”, “Slightly reduced infection risk”, “Very slightly increased infection risk”, and “Very slightly reduced infection risk”. This stratification provides a nuanced understanding of individual variability in COVID-19 susceptibility, which could be critical for personalized risk assessment and management. We further explored the association between *ACE2* polymorphisms and COVID-19 severity. Our analysis extended to 42 genetic markers across 29 genes associated with COVID-19 severity, derived from available literature. These genes are involved in pathways like cytokine signaling, immune regulation, and cellular stress response, all of which are crucial in the pathogenesis of severe COVID-19. Among these markers, 12 (rs11385942, rs2082940, rs2248690, rs4444903, rs324420, rs1801274, rs4073, rs20541, rs2275913, rs832582, rs6721961, and rs3025039) were found to be present in at least 10% of the studied population and were associated with a higher risk of severe COVID-19 complications. Our findings suggest that *ACE2* gene polymorphisms play a significant role in determining COVID-19 susceptibility and severity. Individuals harboring specific *ACE2* genotypes may have an increased risk of developing COVID-19 and experiencing severe complications. This study underscores the importance of genetic factors in COVID-19 and opens avenues for personalized medicine approaches. The identification of high-risk genetic profiles can aid in early intervention strategies and tailored treatment plans, potentially improving patient outcomes. Furthermore, these findings have broader implications for public health policies and pandemic preparedness. Understanding genetic susceptibility can enhance screening strategies and inform vaccine distribution priorities. Additionally, our study lays the groundwork for future research exploring the interaction between *ACE2* polymorphisms and other genetic or environmental factors contributing to COVID-19 outcomes. In conclusion, this study provides compelling evidence of the role of *ACE2* gene polymorphisms in COVID-19 susceptibility and severity. By offering a more detailed genetic landscape of the disease, our research contributes significantly to the ongoing efforts to combat the COVID-19 pandemic through precision medicine and personalized healthcare strategies.

Keywords: Genome mining, COVID-19 severity, *ACE2* polymorphisms, precision health

INTRODUCTION

The emergence of the COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has posed an unprecedented global health crisis. The disease exhibits a wide spectrum of clinical manifestations, ranging from asymptomatic infections to severe respiratory distress and multi-organ failure. This variability in disease severity underscores the critical need to understand the genetic underpinnings of COVID-19 susceptibility and severity. The Angiotensin-Converting Enzyme 2 (ACE2) receptor serves as the primary entry point for SARS-CoV-2 into host cells. Expression of ACE2 is found in various tissues, including the lungs, heart, kidneys, and intestines, highlighting its potential role in the multi-organ effects of COVID-19. Genetic variations in the *ACE2* gene have been implicated in influencing an individual's susceptibility to and severity of COVID-19 [1]. These variations can alter *ACE2* expression levels or modify the protein's structure, potentially influencing the virus's ability to bind and enter cells [2]. To elucidate the associations between *ACE2* polymorphisms and COVID-19 outcomes, we conducted a comprehensive genome mining analysis of 203 genomes from individuals diagnosed with COVID-19. Our study aimed to identify ACE2 polymorphisms associated with the disease and to assess their impact on COVID-19 susceptibility and severity.

MATERIAL AND METHOD

To identify *ACE2* polymorphisms associated with COVID-19 susceptibility and severity, we conducted genome mining on 203 genomes from individuals diagnosed with COVID-19. Genome mining involves analyzing large-scale genomic data to identify genetic variants associated with specific traits or diseases. In our study, we focused on identifying *ACE2* polymorphisms, which are variations in the *ACE2* gene sequence.

Genome Mining Process

i. Data Acquisition: We obtained genome data for 203 individuals diagnosed with COVID-19 from the iPROMISE human genome database.
ii. Genetic Marker Selection: We selected 22 genetic markers across 15 genes linked to COVID-19 susceptibility from existing literature. These markers were chosen based on their documented association with immune response, viral entry mechanisms, and inflammatory processes in viral infections.
iii. Genotyping: We performed genotyping to determine the genetic variants present at each of the selected markers for each individual.
iv. Risk Stratification: Based on their genetic profiles, individuals were stratified into one of seven risk categories: “Moderately increased infection risk”, “Moderately reduced infection risk”, “Roughly average infection risk”, “Slightly increased infection risk”, “Slightly reduced infection risk”, “Very slightly increased infection risk”, and “Very slightly reduced infection risk”.
v. Severity Analysis: We further analyzed the association between *ACE2* polymorphisms and COVID-19 severity. We examined 42 genetic markers across 29 genes associated with COVID-19 severity from available literature. Among these markers, 12 were found to be present in at least 10% of the studied population and were associated with a higher risk of severe COVID-19 complications.

RESULTS AND DISCUSSION

Our genome mining analysis revealed significant associations between *ACE2* polymorphisms and COVID-19 susceptibility and severity. Individuals with specific *ACE2* genotypes exhibited a higher risk of developing COVID-19 and experiencing severe complications. These findings highlight the potential role of genetic factors in modulating an individual's response to SARS-CoV-2 infection.

Susceptibility Analysis

The analysis of 22 genetic markers across 15 genes associated with COVID-19 susceptibility revealed a clear association between specific *ACE2* polymorphisms and an individual's risk of developing the disease. Individuals harboring certain *ACE2* genotypes were found to have a moderately increased or moderately reduced risk of COVID-19 infection compared to those with average infection

risk profiles. These findings suggest that genetic variations in the *ACE2* gene play a significant role in determining an individual's susceptibility to SARS-CoV-2 infection.

Severity Analysis

Our analysis of 42 genetic markers across 29 genes associated with COVID-19 severity identified 12 markers that were significantly associated with an increased risk of severe COVID-19 complications. These markers are involved in pathways crucial for the pathogenesis of severe COVID-19, including cytokine signaling, immune regulation, and cellular stress response. The association between these markers and severe COVID-19 outcomes suggests that genetic factors play a substantial role in determining the severity of COVID-19 infection.

Discussion

Our study provides compelling evidence of the role of ACE2 gene polymorphisms in COVID-19 susceptibility and severity. These findings align with previous research demonstrating the association between genetic variations in ACE2 and an individual's susceptibility to SARS-CoV-2 infection and the severity of COVID-19 outcomes [1,2].

The identification of specific ACE2 polymorphisms associated with an increased risk of COVID-19 and severe complications has important implications for personalized medicine approaches. By understanding an individual's genetic predisposition to the disease, clinicians can tailor preventive measures, treatment strategies, and resource allocation. For instance, individuals with high-risk genetic profiles may benefit from enhanced infection control measures, early intervention strategies, and personalized treatment plans [3,4].

Moreover, our findings have broader implications for public health policies and pandemic preparedness. Understanding genetic susceptibility can inform screening strategies, vaccination campaigns, and resource allocation during pandemics [4,5]. Additionally, our study lays the groundwork for future research exploring the interaction between ACE2 polymorphisms and other genetic or environmental factors contributing to COVID-19 outcomes [1,4,6-7].

TABLE, IMAGE AND FIGURE

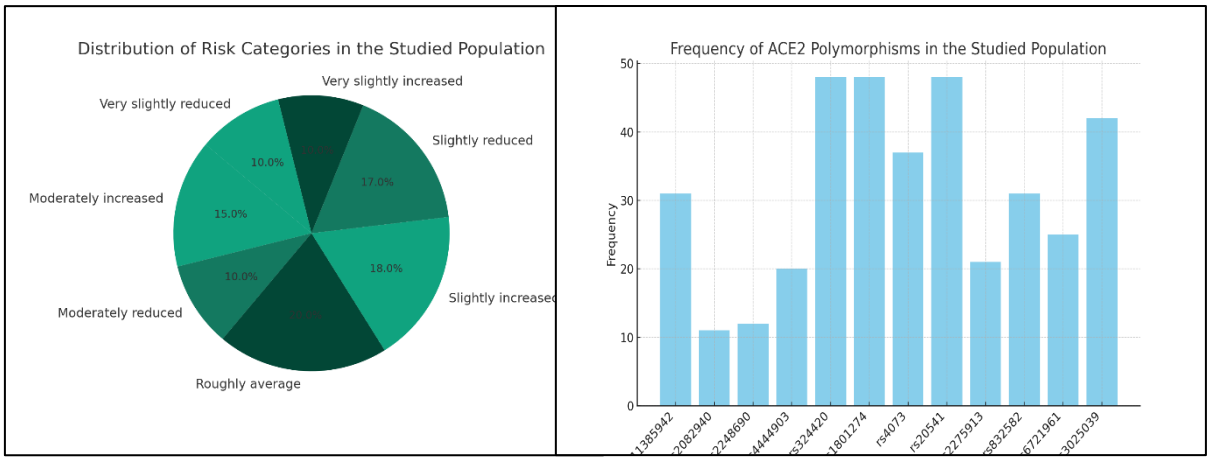

Figure 1: Left: A pie chart showing the distribution of the studied population across the seven risk categories. Right: A histogram displaying the frequency of specific ACE2 polymorphisms within the studied population.

CONCLUSION

Our study provides compelling evidence that genetic variations in the ACE2 gene influence an individual's susceptibility to and severity of COVID-19. Understanding an individual's genetic predisposition can inform personalized preventive measures, treatment strategies, and resource allocation. Additionally, genetic susceptibility data can guide public health policies, such as screening guidelines and vaccination prioritization.

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