Acta Scientific Clinical Case Reports

Volume 4 Issue 6 June 2023

Editorial

Determination of ACE gene polymorphism among COVID-19 Patients as Predictive Marker of Increased Risk of Thrombosis

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Received: January 27, 2023

Published: May 01, 2023

Keywords: Angiotensin-Converting Enzyme (ACE); Thrombosis; COVID-19

The highly contagious new human severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coagulopathies are now recognized as major causes of mortality. SARS-CoV-2 may be a highly prothrombotic virus that alters the coagulation cascade in unknown ways, causing a steady rise in D-dimer as the severity and extent of micro thrombosis rises [1].

COVID-19 has been associated with coagulopathy, particularly micro-clots in the lungs that correlate with disease severity [2]. Recent clinical data have reported that (COVID-19) is associated with a significant risk of thrombotic complications ranging from microvascular thrombosis to venous thromboembolic disease, and stroke. Importantly, thrombotic complications are markers of severe COVID-19 and are associated with multi-organ failure and increased mortality [3]. A study reported that pulmonary embolism and deep vein thrombosis occurred in 20.6% to 49.0% of patients with COVID-19 managed in intensive care units (ICUs) [4]. Uncertainty exists regarding the pathophysiology of the elevated thromboembolic risk in COVID-19 pneumonia. Several mechanisms have been involved in this process including the direct cytotoxic effect induced by the virus, the endothelial cell inflammation, and the dysregulated immune response, which ultimately result in the recruitment of inflammatory cells, platelet aggregation, and activation of the complement and coagulation cascade [5]. The evidence supports the concept that the thrombotic manifestations of severe COVID-19 are due to the ability of SARS-CoV-2 to invade endothelial cells via ACE (angiotensin-converting enzyme) [3,6]. ACE1 and ACE2 cooperate in the (RAS) to balance the local vasoconstrictor/proliferative (ACE1/Ang-II axis) and vasodilator/antiproliferative (ACE2/Ang1-7 axis) actions. This results in the protection of organs and blood vessels by anticoagulants, anti-inflammatory, anti-fibrosis, anti-alveolar epithelial cell apoptosis, and anti-oxidative stress activities antagonizing [7]. Considering the opposite effect between ACE and ACE2, decreased ACE2 receptor gene expression is strongly related to an increase in ACE expression [8].

The counterbalance between ACE and ACE2 activities occurring in COVID-19 may play a crucial role in the thrombo-inflammatory process [5]. ACE1 and ACE2 mutual levels are strongly regulated by common genetic variants in their genes. Wide sex and racial differences in the frequency of ACE1 and ACE2 gene variants have been reported and cluster in subgroups of patients at high risk of COVID-19 poor prognosis (e.g., male sex, Black ethnicity, cardiovascular disease), and they seem to overlap COVID-19 morbidity and mortality rates [9].

ACE1 has an insertion/deletion polymorphism that is characterized by an insertion (allele I) or deletion (allele D) of a 287 base pair marker in intron 16 that results in three different genotypes (DD and II homozygotes or ID heterozygotes). The DD genotype has been found to show the highest serum/tissue ACE1 activity [10]. Different studies have been published on the association of ACE-1 I/D polymorphism with COVID-19 incidence and mortality and may be regarded as a confounder in the spread of COVID-19 and the outcome of the infection [10].

Therefore considering the above findings, the study of the association between ACE I/D polymorphism and levels of both ACE and angiotensin II could represent a genetic risk factor of susceptibility to thromboembolism occurring in COVID-19 disease.

Conflict of Interests

The authors have declared that no any conflict of interests.

Sources of Support

Nil.

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