Bioinformatics and system biology approach to identify the influences of COVID-19 on cardiovascular and hypertensive comorbidities

INTRODUCTION

Recent studies have tracked down that some prior conditions significantly increment the danger of extreme side effects and mortality in COVID-19 patients. These contain pulmonary diseases, cardiovascular diseases, kidney disease, type 2 diabetes, and hypertension. While COVID-19 essentially influences the respiratory system in the beginning stages of the disease, while it additionally influences the cardiovascular system of patients, extraordinarily increasing the risk of fatality. Numerous examinations revealed raised death rates in patients with SARS-CoV-2 infections and increased levels of markers of chronic heart failure. Also discovered hypertension as comorbidity is related with an increased danger of extreme disease with SARS-CoV-2 disease. discovered 32% of COVID-19 patients with another medical issue. studies are needed to identify the interactions between these diseases and COVID-19. Further, the treatments under the examination for COVID-19 may affect cardiovascular disease, hypertension, or other critical comorbidities by impacting the pathways that intercede their interaction with COVID-19.

Angiotensin-Converting Enzyme 2 (ACE2) is known to play an important role in facilitating SARS-CoV-2 cell entry, and this gene is accounted for many human tissues including the intestine, testis, kidneys, heart, and lungs. ACE usually converts Angiotensin I in the renin-angiotensin-aldosterone system (RAAS) of human physiology to Angiotensin II that impact human blood pressure. ACE2 interacts with SARS-CoV2 that may cause vascular dysfunction. ACE inhibitors is used as treatments for hypertension and cardiovascular disease by modulating the RAAS pathway. These drugs inhibit the RAAS and interrupt the performance of ACE and increase the level of ACE2 receptors. In any case, recent investigations found that increased ACE2 levels can be gainful in COVID-19, This serves to show the possible significance of interaction among cardiovascular diseases and hypertension with COVID-19.

In this paper, we considered the interaction of COVID-19 with chronic heart failure (CHF) and idiopathic portal hypertension (IPH), pulmonary arterial hypertension (PAH), and preeclampsia.

CHF is a condition that reduces cardiac output and blood oxygenation insufficiency. **IPH** is a condition of blood pressure in the portal vein and its branches. **PAH** is a case of increased blood pressure within the lungs. **Preeclampsia** is a pregnancy complication that is characterized by hypertensive conditions.

We have found significant cell signaling pathways and gene networks that are commonly associated with these diseases and SARS-CoV-2 infection on human blood cells. The identified pathways and networks are associated with other diseases that may lead to improved therapeutic way for life-threatening SARS-CoV-2 infections.

ABSTRACT

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infected persons that have hypertension or cardiovascular comorbidities have an elevated risk of serious (COVID-19) disease and a high rates of mortality but how COVID-1919 and cardiovascular diseases interact are obscure. We looked to identify a new mechanism of interaction by recognizing genes with expression in SARS-CoV-22 infection that is relevant to the pathogenesis of cardiovascular disease and hypertension. Some research shows the SARS-CoV-22 uses the angiotensin-converting enzyme-2 as a receptor to infect human susceptible cells.ACE2 usually converts Angiotensin I in the renin-angiotensin-aldosterone system to Angiotensin II, which affects blood pressure levels. We use bioinformatics to identify genetic links using MRNA data peripheral blood cells from COVID-19 patients and compared them with blood samples from patients with either chronic heart failure disease or hypertensive diseases. Differentially expressed genes (DEGs) popular to COVID-19 and chronic heart failure, and common to COVID-1919 and hypertension, COVID-1919 does not share a large number of differentially expressed genes with the conditions under consideration. However, those

that were recognized included genes playing roles in T cell functions, such as receptor pathways, cytokines, chemokines, cell stress, type 2 diabetes, and gastric cancer. The result of this study may help in recognizing significant targets of treatment that can combat the progressing pandemic due to SARS-CoV-22 infection.

RELATED WORK

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RESULTS

Differentially expressed genes in whole blood reveal genetic relationships between the COVID-1919, chronic heart failure and hypertensive diseases. We identified the differentially expressed genes (DEGs) for each of these datasets.We identified 12891289 DEGs from the COVID-1919 blood datasets. The number of identified DEGs for CHF, IHP, PAH and PE were 13211321, 247247, 249249, and 127127 respectively.Our observation suggests that COVID-1919 shares more DEGs with

CHF and IHP as compared to the other two conditions. COVID-1919 shares the highest number of DEGs with IPH compared to the other conditions. **DEGs of COVID-1919 immune responses in common with CHF and the hypertensive diseases.** COVID-1919 immune response dataset shares more DEGs with CHF and IPH compared to the other two diseases (PAH and PE). COVID-1919 immune response share only one DEG, which is CCR11 (C–C chemokine receptor type 11), with PE. **Gene set enrichment analysis reveals significant shared signalling and ontology pathways.** We identified the cell signalling pathways that involve the DEGs common to COVID-1919 and each of the other diseases, then determined what other genes may play a role in those pathways. We have combined all the DEGs that discovered from peripheral blood cells and the immune response cells of COVID-1919. We identified the signalling pathways of the commonly DEGs between COVID-1919 and each of the diseases using six global pathway databases include BioPlanet, BioCarta, WikiPathways, KEGG, Reactome and Panther. **Protein–protein interaction analysis identifies functional networks.** We have constructed protein–protein interaction (PPI) network using all common DEGs among COVID-19 and the diseases of cardiovascular and hypertension. We have considered the shared DEGs discovered by analysis of gene expression profiles of blood cells and immune response cells from patients with COVID-19 and the other four diseases. The PPI network has been constructed using a web-based visualisation resource STRING. **Suggested drug and chemical compounds analysis identifies protein–drug and protein–chemical interactions.** The shared DEGs that have been discovered among the interaction of COVID-1919 with chronic heart failure and hypertensive diseases are used in this analysis. We have identified protein–drug and protein–chemical interactions that may influence these genes. We have combined the DEGs identified from both peripheral blood cell and immune response cell populations. We did not find any protein–drug relationship with the DEGs shared by COVID-1919 and PAH.

Methodology

The overall approach in this work consists of seven significant phases. **Gene expression datasets** we have considered two SARS-CoV-22 infected datasets**.**One of the datasets is peripheral blood sample dataset for COVID-19. The blood cell samples were collected from three SARS-CoV-22 patients and three healthy individuals.The second dataset were collected from whole peripheral blood cell samples from COVID-1919 patients and healthy individuals by analysing the immune response using the NanoString Human Immunology Panel. **Gene set enrichment analysis** involves signalling pathway analysis and gene ontology analysis . Signalling pathway and ontology analysis are performed in order to determine the biological significance of the identified DEGs.**Protein–protein interactions** analysis In order to discover associations among the diseases from the perspective of protein interactions, we have identified protein subnetworks using enriched DEGs.**Gene regulatory networks (GRN) analysis** We have identified DEG–miRNA (microRNA) interaction networks and transcription factor(TF)–DEG interaction networks in this analysis. In the case of TF–DEG interaction network analysis, JASPAR database has been used. In GRN analysis, we have used common DEGs to reveal the transcriptional elements and miRNA that regulate DEGs at post-transcriptional level. **Suggested Drug and Chemical Compound Analysis** In this analysis, we have identified protein–drug and protein–chemical interactions using the enriched gene that COVID-1919 shares with cardiovascular and hypertension. We have used Network Analyst to identify protein–drug and protein–chemical interactions.