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Evaluation of the Mucormycosis Risk Factors in COVID-19 Patients in Hospitalized Patients; Rheumatology Ward of Imam Khomeini Hospital: June to November 2021

Authors

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Keywords

COVID-19, Mucormycosis

Abstract

Introduction: Several reports have been presented regarding the presence of mucormycosis in patients with Coronavirus disease 2019 (COVID-19) from all over the world. In COVID-19 patients, mucormycosis can develop rapidly and lead to extensive necrosis in the involved areas. Without rapid and timely diagnosis and appropriate treatment, irreparable complications will occur.

Materials and Methods: This study was a retrospective observational study based on the history of patients who were diagnosed with mucormycosis and COVID-19. The data was tabulated and evaluated for the presence of any risk factors. This study was approved by research Ethics committees of the Imam Khomeini Hospital complex (IR.TUMS.IKHC.REC.1400.352).

Results: 28 patients consisting of 11 women and 17 men with a mean age of 56.39 ± 12.09 were included in this study. Hypertension was reported in 15 patients (53.6%), 22 patients had diabetes Mellitus (78.6%), and 14 of them (28.6%) were recently diagnosed with diabetes. We found out that 26 patients were taking corticosteroids (92.9%). A total of 20 patients (71.4%) had not received the COVID-19 vaccine. The most affected sites of mucormycosis were sinuses, with a prevalence of 23 people (82.1%), orbits with 14 people (50%), rhino-orbits with 12 people (42.9%), and brain, with a prevalence of 3 people (10.7%).

Discussion: We found that middle-aged COVID-19 patients with diabetes mellitus who received steroids were the most susceptible patients to mucormycosis. The most affected sites of mucormycosis were the sinuses, followed by orbits, rhino-orbits, and the brain. We concluded that it is important to diagnose mucormycosis at its early stages of it. As a result, we can reduce soft and hard tissue necrosis with appropriate treatment and avoid irreversible and life-threatening complications.

Conclusion: Patients with COVID-19 infection are susceptible to mucormycosis. Physicians should be aware of the possibility of mucormycosis in these patients, especially in patients with underlying diseases. Early diagnosis and treatment of secondary infections can reduce complications in these patients.

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Sitagliptin, an anti-diabetic agent with anti-inflammatory actions is potential drug for the treatment of COVID-19

Authors

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Keywords

COVID-19, Diabetes, Sitagliptin, DPP-4

Abstract

Introduction: COVID-19 is responsible for the latest contagious pandemic disease that leads to mortality. Peptidomimetic and molecular studies have shown that angiotensin-converting enzyme 2 (ACE-2) and CD26/Dipeptidyl Peptidase-4 (DPP-4) are SARS-CoV-2 receptors and enable the virus to infect cells in the lung and other tissues that express these receptors. Sitagliptin and other DPP-4 inhibitors may be effective medications for COVID-19 by blocking or downregulating the expression of SARS-CoV-2 receptors. Also, sitagliptin can suppress inflammatory cytokines expression. Treatment of type 2 diabetic patients with sitagliptin shows it significantly decreased serum levels of inflammatory markers, such as C - reactive protein and tumor necrosis factor-alpha, and increased anti-inflammatory cytokines as well as interleukin 10. the aim of this study was to assess the roles of sitagliptin, a DPP-4 inhibitor, in the prognosis of COVID-19 infection in patients with type 2 diabetes mellitus.

Materials and Methods: a retrospective cohort study was performed in 2020 in military medical centers affiliated with AJA University of Medical Sciences in Tehran on 220 patients with type 2 diabetes mellitus who were admitted to medical centers with COVID-19 infection. We collected demographic data of patients, including age, gender, drug history, usage of DPP-4 inhibitors, clinical presentations at the time of the first visit, and the disease outcome, including hospitalization duration and need for respiratory assistance.

Results: the study population consisted of 133 males (60.5%) and 87 females (39.5%), with a mean age of 66.13 ± 12.3 years. Forty-four patients (20%) consumed DPP-4 inhibitors (sitagliptin and linagliptin). Patients who were treated with DPP-4 inhibitors required fewer oxygen therapies compared to other cases (76.7% vs. 88.6%, P = 0.04). Patients who were treated with DPP-4 inhibitors had significantly lower hospitalization duration compared to other cases (6.57 ± 2.3 days vs. 8.03 ± 4.4 days, respectively, P = 0.01).

Conclusion: DPP-4 inhibitors could significantly decrease hospitalization days in patients with type 2 diabetes mellitus who were hospitalized for COVID-19.

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mRNA expression of toll-like receptors 3, 7, 8, and 9 in the nasopharyngeal epithelial cells of coronavirus disease 2019 patients

Authors

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Keywords

severe acute respiratory syndrome coronavirus 2, Coronavirus disease 2019, Inflammation, Toll-like receptor, Epithelial cell

Abstract

Introduction: The etiopathogenesis of coronavirus disease 2019 (COVID-19) stem partially from the abnormal activation of the innate and adaptive immune systems. Here in the current investigation, the mRNA expression levels of toll-like receptors (TLRs) were evaluated in the nasopharyngeal epithelial cells from COVID-19 patients.

Materials and Methods: Epithelial cells were obtained using nasopharyngeal swab samples from 90 COVID-19 patients and 50 controls. COVID-19 cases were classified into those without symptoms, with symptoms but not hospitalized, and with symptoms and hospitalized. To determine the mRNA expression levels of TLRs, first RNA was extracted and cDNA was synthesized, and finally Real-time PCR was exerted.

Discussion: It was seen that the transcript levels of TLR3, TLR7, TLR8, and TLR9 were overexpressed in the COVID-19 patients with clinical symptoms needing hospitalization as well as in those with clinical symptoms without needing for hospitalization compared to controls. Upregulation of TLRs was associated with clinical presentations of the patients.

Conclusions: Modulation of TLR3, TLR7, TLR8, TLR9 in the epithelial cells of COVID-19 cases may estimate the disease severity and requirement for hospitalization.

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Induced pluripotent stem cells: Generation Materials and Methods and a new perspective in COVID-19 research

Authors

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Abstract

Induced pluripotent stem cells (iPSCs) exhibit an unlimited ability to self-renew and produce various differentiated cell types, thereby creating high hopes for both scientists and patients as a great tool for basic research as well as for regenerative medicine purposes. The availability and safety of iPSCs for therapeutic purposes require safe and highly efficient Materials and Methods for production of these cells. Different Materials and Methods have been used to produce iPSCs, each of which has advantages and disadvantages. Studying these Materials and Methods would be very helpful in developing an easy, safe, and efficient method for the generation of iPSCs. Since iPSCs can be generated from somatic cells, they can be considered as valuable cellular resources available for important research needs and various therapeutic purposes. Coronavirus disease 2019 (COVID-19) is a disease that has endangered numerous human lives worldwide and currently has no definitive cure. Therefore, researchers have been rigorously studying and examining all aspects of COVID-19 and potential treatment modalities and various drugs in order to enable the treatment, control, and prevention of COVID-19. iPSCs have become one of the most attractive and promising tools in this field by providing the ability to study COVID-19 and the effectiveness of drugs on this disease outside the human body. In this study, we discuss the different Materials and Methods of generation of iPSCs as well as their respective advantages and disadvantages. We also present recent applications of iPSCs in the study and treatment of COVID-19.

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Management of an Emergent Infectious Disease by Routine Laboratory Findings: COVID-19 Wave 1 Prognosis as an Example

Authors

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Keywords

Coronavirus disease 2019 (COVID-19); Laboratory diagnosis, Northeastern Iran; Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); Surrogate biomarkers

Abstract

Introduction: the emerging coronavirus illness of 2019 (COVID-19) was a public health emergency of an infectious disease that exposed the absence of reliable surveillance systems around the globe. This study was performed to find trustworthy substitute markers in diagnosis, risk factors, and anticipation for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Materials and Methods: Demographic, biochemical characteristics, blood indices, and qRT-PCR tests were evaluated on 1,307 people admitted (the capital city in Northeastern Iran, Mashhad).

Results: 1,138 patients (87.07%) were negative for SARS-CoV-2, while 169 patients (12.93%) tested positive. Height was a risk factor for SARS-CoV-2 (P=0.03), and a cutoff of less than 156 cm on the ROC curve exhibited a sensitivity and specificity of 88.3% and 90.8%, respectively. The job was a risk factor; housewives had the highest positive (18%), and healthcare employees had the lowest (3.4%). Education diplomas (32.5%), MD, and Ph.D. (6.1%) showed a positive education efficacy (p=0.011). Though RBC, lymphocyte, eosinophil, neutrophil counts, hemoglobin, ESR, and CRP had significant differences between positive and negative SARS-CoV-2 subjects. Nevertheless, the ROC curve showed that they were not biomarkers for prognosis or diagnosis of infection. However, the cutoff point of platelets lower than 139×109/L had 91.7% sensitivity and 96.9% specificity, and monocyte count higher than 3.5×109/L had 97% sensitivity and 98% specificity for SARS-CoV-2 infection.

Conclusions: the most crucial step in preventing socio-economic harm during the early stages of an acute emerging virus, such as SARS-CoV-2, is to provide trustworthy information (via the media). Then, identifying common surrogate factors to assist medical professionals in monitoring the patients, such as hematologic and biochemical markers, which are available in any underdeveloped area that may be more susceptible to such illness.

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Matrix Metalloproteinases are Involved in the Development of Neurological Complications in Patients with Coronavirus Disease 2019

Authors

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Keywords

Coronavirus disease 2019, Neurological symptom, Matrix metalloproteinases, Inflammatory cytokine, Chemokine, Adhesion molecule

Abstract

Introduction: Evidence shows that Matrix metalloproteinases (MMPs) have been associated with neurological complications in viral infections. Here in the current investigation, we intended to reveal if MMPs are potentially involved in the development of neurological symptoms in patients with Coronavirus disease 2019 (COVID-19).

Materials and Methods: the levels of MMPs, inflammatory cytokines, chemokines, and adhesion molecules were evaluated in the serum and cerebrospinal fluid (CSF) samples from 10COVID-19 patients with the neurological syndrome (NS) and 10COVID-19 patients lacking NS. Monocytes from the CSF samples were treated with TNF-α, and the secreted levels of MMPs were determined.

Results: the frequency of monocytes were increased in the CSF samples ofCOVID-19 patients with NS compared to patients without NS. Levels of inflammatory cytokines IL-1β, IL-6, and TNF-α, chemokines CCL2, CCL3, CCL4, CCL7, CCL12, CXCL8, and CX3CL1, MMPs MMP-2, MMP-3, MMP-9, and MMP-12, and adhesion molecules ICAM- 1, VCAM-1, and E-selectin were significantly increased in the CSF samples ofCOVID-19 patients with NS compared with patients without NS. Treatment of CSF-derived monocytes obtained fromCOVID-19 patients with NS caused increased production of MMP-2, MMP-3, MMP-9, and MMP-12.

Conclusions: Higher levels of inflammatory cytokines might promote the expression of adhesion molecules on the blood-CSF barrier (BCSFB), resulting in the facilitation of monocyte recruitment. Increased levels of CSF chemokines might also help the trafficking of monocytes to CSF. Inflammatory cytokines might enhance the production of MMPs from monocytes, leading to disruption of BCSFB (and, therefore, further infiltration of inflammatory cells to CSF) in COVID-19 patients with NS.

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sFASL is an Inflammatory Marker in COVID-19 Patients; a Clinical And Immune-Epitope Mapping Study

Authors

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Keywords

sFasL, COVID-19, hyperInflammation, computational immunology

Abstract

Introduction: Although soluble Fas ligand (sFasL) has been long known as an apoptosis marker, however, the role of sFasL in Coronavirus disease-2019 (COVID-19) remains unknown. This clinical study reports sFasL as an inflammatory marker in COVID-19 patients.

Materials and Methods: Patients were enrolled in control and three mild, moderate, and critical COVID-19 groups. sFasL was evaluated by Enzyme-linked immunosorbent assay (ELISA). Patients were followed-up for mortality. We assessed IL-6 and CRP as inflammatory markers in COVID-19 patients. COVID-19 patients had higher IL-6 and CRP compared to the control group, which were also associated with the severity of the disease. Bioinformatics analysis of B-cell and T-cell epitopes was performed.

Results: COVID-19 patients had higher IL-6 and CRP compared to the control group. Also, CRP and IL-6 levels were higher in COVID-19 patients with higher severity of the disease.
Cough and fever were the most common clinical presentations. Regression analysis revealed that reduced sFasL levels predicted higher mortality in COVID-19 patients. Our results exhibited that the mean sFasL levels were significantly ($p < 0.05$) reduced in the dead patients compared to the live patients. Multiple B-cell and T-cell epitopes were detected by the IEDB/Discotope tool. Linear epitopes concentrated at aminoacid 26-49, 122-174, and 1-24 .

Conclusions: This is the first report introducing sFasL as an inflammatory marker in COVID-19 patients. Amino acid linkers can be used to combine these epitopes to target sFasL as an immunotherapeutic approach. Studies targeting sFasL through protein design and preclinical studies of inhaled anti-sFasL therapy are warranted. Future studies suggested.

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Prediction of Sars-Cov-2 Orf1ab Protein Allergenicity By Immunoinformatic

Authors

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Keywords

COVID-19, ORF1ab, allergen, immunoinformatic

Abstract

Introduction: Hypersensitivity reactions to SARS-CoV-2 have been shown by various studies. ORF1ab (open reading frame1ab) is the biggest ORF of the severe acute respiratory disease coronavirus 2 (SARS-CoV-2) genome. Also, ORF1ab protein is primarily translated into infected cells. Moreover, ORF1ab is heritably constant and might have valuable conserved epitopes suitable to make effective vaccines for the control of numerous SARS-CoV-2 variations. in this study, COVID-19 ORF1ab protein allergenicity was assessed by immunoinformatic.

Materials and Methods: Amino acid sequences of SARS-CoV-2 ORF1ab protein were found in the NCBI database in FASTA format. Then, the allergenicity of SARS-CoV-2 ORF1ab protein was assessed by Allergen FP server V.1.

Results: ORF1ab protein of SARS-CoV-2 showed allergenicity as was defined by allergen FP server V.1.

Conclusions: According to our results, the ORF1ab protein of COVID-19 was potentially an allergen. Hypersensitivity reactions to some SARS-CoV-2 vaccines have been reported by various studies. Also, inflammation in COVID-19 has been shown by several investigations. Hypersensitivity and inflammation shown in COVID-19 may be partly due to ORF1ab protein allergenicity. However, ORF1ab protein, having valuable conserved epitopes, seems suitable to make effective vaccines for the control of several SARS-CoV-2 variants. in order to produce safe and efficient anti-SARS-CoV-2 vaccines from ORF1ab protein, recognition and removal of its allergenic epitope (s) is necessary.

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Increasing Autoimmune Markers Among ICU-Hospitalized COVID-19 Patients

Authors

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Keywords

COVID-19, ICU-hospitalized patients, autoimmune markers

Abstract

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes multi-organ damage due to the induction of inappropriate immune responses, particularly lung tissue fibrosis. To evaluate the consequence of the deterioration of the immune system, autoimmune markers were assessed in this study.

Materials and Methods & Materials: in a case-control study, 108 COVID-19 patients who were admitted to the ICU and 158 outpatients with SARS-Cov-2 RT-qPCR positive test and mild clinical symptoms were included. The demographic and hematologic variables and presence of the main autoantibodies in sera of 40 eligible ICU-hospitalized COVID-19 patients and 40 COVID-19 outpatients were assessed. Out of 108 COVID-19 ICU-hospitalized patients, 40 subjects were selected as the control group (40/158) who did not have any underlying diseases before hospitalization, according to the self-declaration and clinical records at the time of admission.

Results: The Results demonstrated that the main CBC indices, such as RBC and platelets, decreased dramatically in ICU-hospitalized patients. Furthermore, the autoantibody profiles were positive in 45% and 15% of ICU admitted patients for ANA and ANCA, respectively. in ICU patients, anti-PM/Scl 100 or AMA-M2 is 33%. Anti SS-A, anti-SS-B, anti-Ro-52, and anti-Jo- in 11/5% for each one were reactive. Other autoantibodies of the ICU group are as follows: CENP (5/6%), Rib-protein (5/6%), and nucleosome (5/6%). However, only two subjects in the control group had positive Results for SS-A and SS-B (5%).

Conclusion: Inducing such particular autoantibodies by the virus can justify the multi-organ involvement and severity of the disease in ICU patients, which may also cause other organ involvement in the long term.

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Assessment of mIR-200c-3p and miR-421-5p Levels During Immune Responses Among Admitted And Recovered COVID-19 Patients

Authors

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Keywords

miR-200c, miR-421, COVID-19

Abstract

Introduction: Angiotensin-converting enzyme 2 (ACE2), as a main receptor, interacts with the spike of SARS-CoV-2. Two key microRNAs (miRs), miR-200c-3p and miR-421-5p, are well-known to regulate ACE2 gene expression, so alterations in the expression of these miRNAs may affect the outcomes of COVID-19 infection. Therefore, we investigated whether miRNAs directing ACE2 expression altered in the SARS-CoV-2 infection.

Materials and Methods: Thirty patients with COVID-19 participated in the study, and whole blood collection was provided. Then, the gene expression of miR-200c-3p and miR- 421-5p, inflammatory cytokine IL-6, and regulatory T cells' markers (CD4, CD25, and Foxp3) were evaluated using quantitative real-time PCR method at the time of admission and discharge.

Results: At the time of admission, the levels of miR-200c- 3p and miR-421-5p, as well as CD4, CD25, and Foxp3 gene expression were noticeably reduced, whereas IL-6 gene expression remarkably boosted in the circulating of infected patients. Meanwhile, by the time of discharge, the expression levels of the genes were significantly diminished. Moreover, Pearson correlation analysis indicated that IL-6 expression was negatively associated with Foxp3 and miR-200c-3p expressions, although miR-421-5p expression positively correlated with miR-200c-3p expression upon admission.

Conclusion: By manipulating miR-200c-3p and miR-421-5p expressions and regulatory the ACE2 levels, it is plausible to modulate the inflammation through IL-6 reduction and maintenance tolerance hemostasis duringCOVID-19 infection.

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Effect of Extracellular Neutrophil Trap in the Coronavirus Pathophysiology

Authors

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Keywords

Coronavirus disease, neutrophil extracellular traps (NETosis), thrombosis

Abstract

Introduction: Coronavirus disease is a highly contagious disease with high mortality and risk of death, which is more progressive in patients with compromised immune systems or underlying medical problems. However, the cells involved in the innate immune system play a decisive role in disease progression and complications. Pathogen entrapment is a critical role of neutrophil extracellular traps (NETosis). This process involves the widespread release of fibrous structures composed of cytosolic proteins and granular contents held together by a network of released chromatin. This network can prevent pathogens from spreading by trapping them. in addition, NETosis harms the host by producing toxic agents and causing thrombosis. Therefore, this phenomenon may act as a double-edged sword. Considering the rapid spread of corona disease, it is very necessary to investigate the role of NETosis in infected patients.

Materials and Methods: This review intended to elucidate the contribution of NETosis to demonstrate its possible association with increased risk of thrombogenicity and to contribute to the development of new therapeutic approaches in the battle against this viral disease.

Results: The data indicate that CRS is associated with the progression and severity of COVID-19. However, COVID-19 sera were revealed to be a potent stimulator of NETosis after adding to normal neutrophils. It is reported that a variety of stimuli can trigger neutrophils toward NETosis.COVID-19 is also suggested as a pro-NETotic element that may trigger NETosis following epithelial cells' damage. NETs can be generated and initiate the coagulation pathway as well.

Conclusions: Collectively, this review suggests that NETosis, as an important interface between CRS and thrombosis (especially in patients with ARDS), should be considered to develop more effective therapeutic approaches.

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Common Microbial Agents in Asthmatic Children with Respiratory Infections and Productive Cough

Authors

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Keywords

Asthma attack, bacterial, viral infections, allergy

Abstract

Introduction: Microbes can influence the development and somehow on triggering of asthma attacks. They have threatened and affected human life, especially children, for centuries. Therefore, in this study, the more significant microbial infections which trigger asthma attacks in children were evaluated.

Materials and Methods: A total of 41 nasopharyngeal and oro-pharyngeal swabs were obtained from the Pediatric Allergy Clinic of two educational hospitals and sent to a Molecular Laboratory for evaluation of 21 bacterial and viral respiratory pathogens using the qPCR-TaqMan method.

Results: The main bacterial infections were S.aur 18/41 (43.9%), S.pneu 16/41 (39%), C.pneu 12 /41 (29.3%), and HIB 17/41 (41.5%), while the most viral infections were and HRSV 3/41 (7.3%) and FluB, HRV, HMPVA.B, HPIV-2,3,4, HcoV-63, and HcoV-229 in 2 cases (4,9%), in asthmatic children. Although bacterial infections were more common in both genders, the frequency of those agents was a statistical difference between the girls' and boys' populations (P=0.02). There were positive correlations between S. pneu infection with an asthma attack and bronchitis (P= 0.02 and P= 0.001, respectively). Furthermore, a positive correlation was found between AV and RSVA.B infections with allergic rhinitis (P= 0.02 and P= 0.001, respectively).

Conclusion: In Conclusion, it is more likely that in a populated region with a moving population, bacterial respiratory infections, particularly HIB, S.aur, and S. pneu, were more common, however, and consistent with other studies of HRSV and Flu. B has been the dominant viral infection in asthmatic attacks.

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MicroRNAs in SARS-CoV-2 and Neuroinflammation: In silico Analysis

Authors

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Keywords

MicroRNA, neuroinflammation, SARS-CoV-2, GAPDH, hsa-miR-325-3p

Abstract

Introduction: Since the COVID-19 pandemic, limited case studies have reported the co-occurrence of neuroinflammation and SARS-COV-2 infection. In the present in silico study, researchers have identified common microRNAs between these two diseases.

Material and method: By using the diagenetic database, the COVID-19 and Neuroinflammation-related genes were extracted. Also, through the Venn diagram using, the shared genes were found. The Cytoscape software was applied to identify the most interacted genes, and the target scan database was utilized to find related microRNA.

Results: The Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was obtained as the shared gene. Additionally, the microRNA, including hsa-miR-325-3p, can be regarded as the most critical shared expression regulator between neuroinflammation and SARS-COV-2.

Conclusion: Overall, according to former evidence, SARS-CoV-19 has a variety of effects on the brain, including direct infection of neural cells with SARS-CoV-2, severe systemic inflammation that floods the brain with pro-inflammatory agents, causing nerve cell damage, global brain ischemia and respiratory failure, thromboembolic strokes and psychological stress associated with increased intravascular clotting. Also, our Results indicated the genetic connection between SARS-CoV-2 and neuroinflammation. There is a substantial increase in the incidence of neurodegenerative diseases and dementia due to all these factors.

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Investigating the long-term physical, psychological, and social damage of patients infected with COVID-19

Authors

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Keywords

post-Corona, physical injury, psychological injury, social injury

Abstract

Introduction: Currently, one of the biggest challenges for different societies is the complications of the emerging epidemic of COVID-19. The damage related to this epidemic is not only related to the treatment process of the patients, but many complications remain in people suffering from this disease all over the world. This research was conducted with the aim of investigating the long-term physical, psychological, and social damages to patients infected with COVID-19 in 2022.

Method: the study was conducted as a systematic review in the period of 2019-2022. in line with the search, the Keywords of coronavirus, COVID-19, physical damage, psychological and social damage, and post-corona were used to search Scopus, ScienceDirect, PubMed, Scholar, SID, and Magiran databases. A total of 3740 articles were found. After removing the articles that were not related to the objectives of the research, finally, 100 articles were included in the research and were fully examined.

Results: the review of studies showed the prevalence of various physical, mental, and social problems among these people. The most common physical effects observed include shortness of breath, fatigue, muscle pains, headaches, neurological disorders, and reduced physical capacity of the body. The most common psychological problems include anxiety, depression, post-traumatic stress disorder, sleep disorders, and anger. In relation to social problems, social stigma, and family problems have been the most common.

Conclusion: the review of studies showed that in the post-corona era, we are witnessing many cases of mental, social, and physical injuries among patients with COVID-19. Therefore, it is necessary to make appropriate plans to identify possible injuries, perform necessary screenings, and plan effectively to treat these injuries.

3rd International Congress on Inflammation

Survey of Death Anxiety in Pre-Hospital Personnel of Qom University of Medical Sciences During the COVID-19 Era

Authors

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Keywords

death anxiety, pre-hospital, pandemic, COVID-19

Abstract

Introduction: pre-hospital personnel is frequently faced with death and dying patients due to the nature of their job. Death anxiety in these people may be associated with depression, generalized anxiety, and suicidal thoughts, which may impair their performance. Therefore, the present study was conducted with the aim of investigating the death anxiety of pre-hospital personnel during the COVID-19 era.

Materials and Methods: This cross-sectional study was conducted on 185 pre-hospital personnel of Qom University of Medical Sciences in January 2021. Sampling was done by simple random method. The data collection tool in this study included the Introduction information checklist and Templer Death Anxiety Questionnaire. Data analysis was performed with the help of SPSS16 software. Descriptive tests, the t-test, ANOVA, and regression were used.

Results: the average age of the participants, work experience, and overtime hours were 35.15±8.8, 11±7.25, and 115.46±45.33, respectively. More than half of the participants had a bachelor's degree. More than two-thirds of people were married. There were people with shifts in circulation. The average score of death anxiety was 6.48 ± 3.0. the average score of death anxiety in the dimensions of fear of death: 1.31±1.02, fear of pain and disease: 1.06±1.42, thoughts related to death: 0.706±0.77, transient and short time: 1.80±0.92, and fear of the future 1.06±0.74. Based on the results of the multivariate regression test, the variables of employment status had an effect on the death anxiety of pre-hospital personnel (R=0.278, p=0.032).

Conclusion: The results of this study demonstrated that death anxiety in the COVID-19 era is at a low level among pre-hospital personnel during the COVID-19 pandemic crisis. Therefore, educational intervention programs are necessary to reduce death anxiety and its complications. So, it is suggested to conduct qualitative studies to eliminate the death anxiety of pre-hospital personnel in crises.

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The Prognostic Value of s100a Calcium-Binding Protein Family Members in Predicting Severe Forms of COVID-19

Authors

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Keywords

Coronavirus disease 2019, Inflammation, S100A4, S100A9, S100A10

Abstract

Introduction: Excessive inflammation has been implicated in the immunopathogenesis of coronavirus disease 2019 (COVID-19). in the current study, the involvement of S100 calcium-binding protein S100A4, S100A9, and S100A10 in the inflammatory settings ofCOVID-19 patients was evaluated.

Materials and Methods: Peripheral blood samples were obtained from 65 COVID-19 subjects and 50 healthy controls. From the blood samples, RNA was extracted, and cDNA was synthesized, and then the mRNA expression levels of S100A4, S100A9, and S100A10 were measured by Real-time PCR.

Results: the mRNA expression of S100A4 (fold change [FC] = 1.45, P = 0.0011), S100A9 (FC = 1.47, P = 0.0013), and S100A10 (FC = 1.35, P = 0.0053) was significantly upregulated inCOVID-19 patients than controls. the mRNA expression of S100A4 (FC = 1.43, P = 0.0071), (FC = 1.66, P = 0.0001), and S100A10 (FC = 1.63, P = 0.0003) was significantly upregulated in the severeCOVID-19 subjects than mild-to-moderate subjects. There was a significant positive correlation between the mRNA expression of S100A4 (ρ = 0.49, P = 0.030), S100A9 (ρ = 0.55, P = 0.009), and S100A10 (ρ = 0.39, P = 0.040) and d-dimer in theCOVID-19 patients. the AUC for S100A4, S100A9, and S100A10 mRNAs were 0.79 (95% CI 0.66–0.92, P = 0.004), 0.80 (95% CI 0.67–0.93, P = 0.002), and 0.71 (95% CI 0.56–0.85, P = 0.010), respectively.

Conclusions: S100A4, S100A9, and S100A10 play a role in the inflammatory conditions in COVID-19 patients and have the potential to the prognosis of the severe form of COVID-19. Targeting these modules, hopefully, might confer a therapeutic tool in preventing severe symptoms in COVID-19 patients.

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The Relationship Between Serum Levels of Interleukin-2 And IL-8 with Circulating microRNA-10b in Patients with COVID-19

Authors

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Keywords

COVID-2019, MicroRNA, Cytokine Storm, IL-2, IL-18

Abstract

Introduction: the role of cytokine storm in the immunopathogenesis of coronavirus disease 2019 (COVID-19) has been implicated. The aim of this study is to determine the association of microRNA (miRNA)-10b and serum levels of IL-2 and IL-8 in patients with COVID-19.

Materials and Methods: Blood samples were obtained from 33 COVID-19 patients and 29 healthy subjects. After RNA extraction and cDNA synthesis, the transcript level of miR-10b was determined by Real-time PCR. in addition, the serum levels of IL-2 and IL-8 were measured in subjects using ELISA.

Results: the patient group comprised 33 patients with COVID-19 (62.4 ± 3.7 years old), 13 (39%) males and 20 (61%) females. In the control group, 29 subjects (56.6 ± 1.6 years old), 9 (31%) males, and 20 (69%) females were included. The expression of miR-10b was significantly downregulated in the peripheral blood of COVID-19 patients in comparison to the healthy controls (fold change= 0.12, P< 0.0001). the levels of IL-2 (P< 0.001) and IL-8 (P< 0.001) were significantly increased in the serum samples ofCOVID-19 patients compared to the healthy subjects. the expression level of miR-10b was correlated significantly with the serum levels of IL-2 and IL-8 as well as with the age of patients, ESR, and CRP levels.

Conclusions: miR-10b is downregulated in COVID-19 patients and might result in increased levels of IL-2 and IL-8, hence contributing to cytokine storm.

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Is There Any Relationship Between Serum Zinc Levels and Angiotensin-Converting Enzyme 2 Gene Expression in Patients with Coronavirus Disease 2019?

Authors

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Keywords

Zinc, ACE2, COVID-19

Abstract

Introduction: the level of angiotensin-converting enzyme 2 (ACE2) expression in different tissues is essential in the sensitivity, symptoms, and consequences of COVID-19 infection. It seems that zinc is involved in the structure of the ACE2 enzyme has been identified; nonetheless, the relationship between ACE2 expression and zinc serum levels in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected patients is still unclear. This study aimed to evaluate the expression of ACE2 in peripheral blood-derived immune cells of COVID-19 patients and its relationship with serum zinc levels.

Materials and Methods: Thirty healthy subjects and thirty patients with COVID-19 were enrolled in this study. COVID-19 infection was confirmed by positive real-time polymerase chain reaction (RT-PCR) and radiological data. Peripheral blood samples were taken from healthy subjects and COVID-19 patients. Whole blood samples were also used to measure ACE2 gene expression by RT-PCR technique. The correlation matrix evaluated the relationship between ACE2 expression, serum zinc levels, and other related variables.

Discussion: the outcomes showed no considerable alteration in serum zinc levels between patients and the control group. Likewise, the ACE2 gene expression **Results** showed a significant decrease in this receptor's expression in COVID-19 patients compared with the healthy subjects. A significant positive correlation was observed between serum zinc level and ACE2 gene expression in patients with COVID-19.

Conclusion: the immune system seems to reduce the mRNA expression of the ACE2 in the peripheral blood leukocytes following SARS-CoV-2 infection. Moreover, zinc deficiency can make patients more susceptible to SARS-CoV-2 infection.

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COVID-19 and Thrombocytopenia; a Bioinformatic Approach

Authors

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Keyword:

SARS-CoV-2, thrombocytopenia, Oncostatin M, bioinformatic

Abstract

Introduction: Since the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) pandemic emerged, growing documents have indicated the incidence of coagulation disorders, especially thrombocytopenia among COVID-19-infected patients. the current study aims to describeCOVID-19-dependent thrombocytopenia properties and investigate the practical factors in platelet dysfunction via a bioinformatics approach.

Material and Methods: Using GEO, the related gene sets to thrombocytopenia andCOVID-19 were extracted. To identification of similar genes, the Venn diagram tools were utilized. Also, in order to the identification of correlated pathways, the enrich r website was applied.

Results: Our data revealed that Oncostatin M (OSM) could be a related genetic key between thrombocytopenia andCOVID-19. During SARS-CoV-2 infection, the pathways, including the JAK-STAT signaling pathway, Cytokine-cytokine receptor interaction, and PI3K-Akt signaling, must be regarded as trigger factors to induce thrombocytopenia amongCOVID-19 patients.

Conclusion: Dysregulated immune responses affect coagulopathies' incidence among COVID-19 patients; however, SARS-COV2-dependent thrombocytopenia could be regarded as multifactorial pathology. The knowledge advancement about SARS-COV2-dependent thrombocytopenia might have valid diagnostic, prognostic, and therapeutic criteria for SARS-COV2 treatment.

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Evaluation of Two Type I IFN-Induced Genes (Ly6e And Usp18) Gene Expression And Association with the Severity of Clinical Symptoms in COVID-19 Patients

Authors

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Keywords

COVID-19, severity of clinical symptoms, type one interferon, ly6e, usp18

Abstract

Introduction: COVID-19 disease is a pandemic with high spreading power, and a wide range of clinical symptoms and lack of definitive treatment have been a challenge for mankind in recent years. The antiviral response of type 1 interferon against the SARS-COV-2 virus is one of the most important pathways of the innate immune system in dealing with this disease. The purpose of this study is to investigate the relationship between the expression of two genes, ly6e, and usp18, with the severity of clinical symptoms in patients with COVID-19.

Material and method: Peripheral blood samples were prepared from 186 patients (40 in the control group, 42 in the outpatient group, and 104 in the inpatient group and the inpatient group included 43 in the moderate group, 30 in the severe group, and 31 in the critical group) and their DNA was extracted. The expression of ly6e and usp18 genes was measured by the real-time PCR method. cDNA samples were first amplified using specific primers. Data analysis was done using Chi-squared, Mann-Whitney, and Kruskal-Wallis tests in SPSS software (version 26). a significance level of 0.05 was considered.

Results: the expression of the ly6e gene was significantly (p=0.008) decreased in the hospitalized group compared to the control group. No significant difference was seen in the expression of the usp18 gene among the studied groups.

Conclusion: Proper expression of ly6e protein can be related to controlling the severity of clinical symptoms of COVID-19 disease.

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Evaluation of the Humoral Immune Response Elicited By Two Vaccine Platforms Against SARS-CoV-2

Authors

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Keywords

SARS-CoV-2, Vaccines, Humoral immunity

Abstract

Introduction: To date, several vaccine platforms have been designed with the common goal of eliciting an effective immune response against SARS-CoV-2. The purpose of this study was to evaluate the humoral immune response in Iranian people vaccinated with both inactivated virus vaccines and vector vaccine platforms.

Materials and Methods: In total, 360 vaccinated individuals with inactivated virus vaccines (BBIBP-CorV and Covaxin) and vector vaccine platforms (AstraZeneca and Sputnik V) enrolled in the study. Serum samples were collected for each volunteer on days 14 to 21 after vaccination, and anti–SARS-CoV-2 spike receptor-binding domain (RBD) IgG concentrations were analyzed by enzyme-linked immunosorbent assay (ELISA).

Results: Higher antibody titers were observed in participants vaccinated with vector vaccines compared with those vaccinated with inactivated virus, especially in subjects who received two doses of AstraZeneca. (AstraZeneca: 204.19 U/mL [95% CI, 175.5-232.2] vs Sputnik V :114.67 U/mL [95% CI, 99.54-129.8]; P = 0.007). It was also observed that antibody titers were not significantly different between the two groups receiving inactivated vaccines (p= 0.86). Our results indicated that 28% of the population vaccinated with Covaxin and 32% of people vaccinated with BBIBP-CorV had shown no response to the vaccine. There was also a statistically not significant difference between age, BMI, and gender with antibody level in each group of vaccines (p > 0.05).

Conclusions: Our study showed that viral vector-based vaccines produce higher levels of neutralized antibodies than inactivated vaccines, and the rate of non-response is less in them. Therefore, they may be the better option for vaccination against SARS-COV2.

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Serum Levels of Hsp27 Protein in Patients with COVID-19 And Its Relationship with Severity of Disease

Authors

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Keywords

HSP27, COVID-19, SARS-CoV-2, Heat Shock Proteins

Abstract

Introduction: After the outbreak of the COVID-19 pandemic in recent years, the molecular mechanisms involved in the infection with the newly emerged virus SARS-CoV-2 have been investigated for a better understanding of this disease in order to help its prevention, diagnosis, and treatment. In the meantime, one of the attractive issues is to investigate heat shock proteins as one of the host factors in this disease. HSP27 plays a critical role in cell cycle promotion, apoptosis, immune responses, and viral life cycles. Although many viral proteins have been shown to cooperate with HSP27 in the regulation of virus-induced autophagy, type I IFN, and NF-κB signaling pathways, its role during SARS-Cov-2 infection is unclear. The current study provides insight into the variation of HSP27 protein levels in patients with mild and moderate-to-severe symptoms of COVID-19 compared to the healthy control group.

Materials and Methods: in this study, 90 patients with COVID-19 (45 patients with moderate to severe symptoms and 45 patients with mild symptoms) and 42 patients as the healthy control group were selected. Afterward, written informed consent was obtained from all participants. The serum HSP27 levels of the subjects were measured using the commercially available ELISA kit.

Results: Based on the results obtained, although the average serum levels of HSP27 in males with moderate to severe symptoms were significant (95% confidence interval value) compared to those of the control group, the average serum levels of HSP27 in patients with mild symptoms and patients with moderate to severe symptoms, no statistically significant difference was observed in general.

Conclusions: According to the results of the present study, although it seems that this molecule cannot be considered as a biomarker in COVID-19, it is possible that conducting future studies could help clarify the molecular role of HSP27 in infections with the SARS-CoV-2 virus.

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Clinical, Laboratory Characteristics and the Associated Factors of Mortality in Patients with COVID-19 Infection Hospitalized in a Tertiary Hospital

Authors

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Abstract

Introduction: Identification of clinical features and associated factors of mortality of COVID-19 infection is important for earlier diagnosis and risk factors. The present study was designed to determine the clinical characteristics and outcomes of patients who have been hospitalized in a tertiary care hospital.

Materials and Methods: This retrospective cross-sectional study comprised only patients who required hospitalization because of COVID-19. The diagnosis was confirmed by using a polymerase chain reaction test. All patients received standard-of-care treatment. The patients were stratified according to disease outcomes into survivors and nonsurvivors, and the two groups were compared to determine associated factors of mortality.

Results: 88 patients (female 44%) with a median age of 63 years (range 29-87) were studied. Seventeen (19.3%) patients expired. Mean hemoglobin, serum CRP, alkaline phosphatase, and procalcitonin levels in non-surveys were significantly higher than in survivors (p-values =.0.03, 0.02, 0.03, and 0.01, respectively). The mean percentage of white blood cells in nonsurvivors was significantly higher, but the percentages of lymphocytes, neutrophils, and platelets did not differ significantly. Other markers of inflammation, such as ESR, ProBNP, IL-6, TNF-a, and ferritin, did not differ between the two groups. Using multiple regression analysis, after adjustment for covariates including demographic features, coexistent chronic morbidities such as diabetes, hypertension, obesity, renal, cardiovascular diseases, and history of cancers, the differences decreased to no significant levels.

Conclusion: These findings indicate high mortality of hospitalized COVID-19 infection. Studies with larger samples are required to address risk factors of mortality.

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Frequency of $CD4^{+}CD25^{+}CD127^{-}$ Regulatory T Cells in Peripheral Blood of Pediatric Patients with Multisystem Inflammatory Syndrome in Children

Authors

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Abstract

Introduction: Multisystem Inflammatory Syndrome in children (MIS-C) is a rare but devastating complication of COVID-19 presenting 4–6 weeks after infection as high fever, organ dysfunction, and strongly elevated markers of inflammation. Tregs down-regulate immune responses in inflammatory and autoimmune diseases. This study aimed to investigate the levels of $CD4^{+}CD25^{+}CD127^{-}$ Tregs in children with MIS-C.

Materials and Methods:
The frequency of Tregs was measured by flow cytometry in 10 children with Mis-C(acute phase and before any treatment) and 6 healthy children with a history of COVID-19 infection 4-6 weeks before enrollment as a control group. This study was conducted between March 1 and October 30, 2021, in Imam Ali Karaj Hospital (Iran)3

Results: The mean age of patients was 8.21 ± 3.86. all patients had elevated inflammatory markers and lymphopenia, and 78.5% had IgG antibodies against COVID-19. There was no significant difference between patients with Mis-C and healthy control children in the frequency of Tregs (P=0.328). Attempts to correlate Tregs with other markers, such as neutrophil count and lymphopenia, were insignificant.

Conclusion: Our findings do not support an important role for Tregs count in the acute phase of Mis-C disease.

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The Effect of Ace1 I/D Polymorphism in the Outcome of COVID-19 Patients: A Case-Control Study

Authors

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Keywords

Polymorphism; Insertion/deletion, ACE, COVID-19

Abstract

Introduction: Due to the recent pandemic ofCOVID-19, many countries have experienced a massive number ofCOVID-19 cases and deaths. the etiology of a wide spectrum of symptoms is still under debate and is affected by multiple variables. Risk factors such as sex, age, and underlying diseases play an important role in this variability. Nevertheless, host genetic variants may also be a major influence on the outcome of the disease. Hence, this study aimed to examine the association of ACE1 gene Insertion/Deletion (I/D) polymorphism (rs1799752) withCOVID-19 severity.

Materials and Methods: This study included 898 COVID-19 patients and a control group of 202 healthy individuals across several major cities in Iran. The blood sample and clinical data were collected, and ACE1 I/D polymorphism was determined via a polymerase chain reaction. Serum levels of CRP, IL-6, and ACE1 were obtained from the medical records.

Results: We found that age, cigarette smoking, and underlying diseases were associated with an increased risk of mortality and severity of the disease. We observed that the frequency of II + ID genotypes significantly correlated with the risk of ICU admission (P = 0.042), intubation (P=0.017), and mortality of COVID-19 patients (P=0.049). Even after adjustment, logistic regression demonstrated that this significant association remained true for the above variables at OR=1.9, OR=2.6, and OR= 2.1, respectively. Also, in expired (p=0.026) and intubated (p=0.019) groups with II + DI genotypes, the mean level of CRP was significantly higher than in the DD genotype group. Furthermore, in both intubated and expired groups, the mean serum level of ACE1 was higher compared with non-intubated and alive groups who had II or II + ID genotypes.

Conclusion: Our finding suggests that II + ID genotypes of ACE1 polymorphism could potentially influence the outcome ofCOVID-19 in the Iranian population.

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Association of TLR-7 Genes Polymorphism with Severity to COVID-19

Authors

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Keywords

TLR7; SARS-CoV-2; Single-nucleotide polymorphisms

Abstract

Introduction: Recently, SARS-CoV-2 infection has become the leading global public health problem. The innate immunity through the Pattern recognition receptors (PRR), including Toll-like receptors (TLR) and RIG-like receptors (RLR), play crucial roles in the antiviral immune response. Genetic polymorphisms can influence this antiviral immune response. The present study aimed to identify three single nucleotide variants of TLR7, including rs179008 (A>C), rs3853839 (C>G), and rs179009 (A>G) gene associated with the severity of COVID-19.

Materials and Methods: This study recruited 165 patients with severe COVID-19 and 182 with mild COVID-19. Genomic DNA was extracted from peripheral blood leukocytes of patients to determine the genotypes TLR7 -rs179008 (A>C), rs3853839 (C>G), rs179009 (A>G)- gene using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.

Results: No significant association was found in the genotype or allele distribution of selected SNPs of the TLR7 gene in patients with severe and mild COVID-19.

Conclusion: Our results showed that these SNPs are not associated with COVID-19 severity in the Kermanshah population, Iran.

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Antibody Production After COVID-19 Vaccination in Primary Immunodeficiency Patients

Authors

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Keywords

Primary Immunodeficiency (PID), COVID-19 Vaccination, Antibody Production, Sinopharm Vaccine

Abstract

Introduction: Vaccinating patients with primary immunodeficiency (PID) against COVID-19 is a rational approach to counteract the disease in these patients. Few studies have evaluated COVID-19 vaccine efficacy in PID patients. This study compared antibody production after COVID-19 vaccination in 42 PID patients and 32 controls.

Materials and Methods: Three Materials and Methods were used to measure antibody production, including the SARS-CoV-2 neutralization test, anti-SARS-Cov-2 immunoglobulin titer, and anti-SARS-Cov-2 neutralizing antibody test (ChemoBind).

Results: the patients' ages ranged from 19 to 78, with a median of 33. The median age for the controls was 41 years. PID cases included hereditary angioedema (n=19), common variable immunodeficiency (n=8), CGD (n=7), neutropenia (n=3), hyper-IgE syndrome (n=2) and X-linked agammaglobulinemia. of the 42 patients, 40 (93%) had received Sinopharm. The findings of this study suggest that PID patients in most subgroups had antibody production similar to that of controls. Lower hospitalization rates were also observed in these patients.

Conclusion: These effects could be explained by the restrictive measures taken by PID patients, the non-significant role of B cells and antibody protection against COVID-19, or the lower likelihood of immune system overactivation. More evidence is needed to establish effective guidelines on the type and schedule of vaccines in different PID subgroups.

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Ct Values Predict COVID-19 Severity and Mortality but Not Correlated with Laboratory Markers

Authors

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Abstract

Introduction: A considerable number of studies have evaluated the possible utility of cycle threshold (Ct) values as a predictor factor of COVID-19 severity and patients' outcome. Given the inconsistent available results, we aimed to evaluate the association between SARS-CoV2 CT values and disease severity, inflammatory markers, and outcomes in Iranian patients with COVID-19.

Materials and Methods: A retrospective study of patients with COVID-19 hospitalized from September 2020 to October 2021 (n=528) was conducted. Demographic, clinical, and laboratory data of patients were retrieved from the electronic medical records. CT values were analyzed as a continuous variable and also after subcategorizing into three groups: low (CT values <20), medium (CT values =20-30), and high (CT values >30).

Results: of 528 patients (45.1% female, 54.9% male) in age ranges 13 to 97 years (mean±SD: 57±17 years), 109 patients had low CT values, 312 patients had medium, and 107 patients had high CT values. Patients with low CT values were more likely to present critical COVID-19 (p=0.006), require invasive mechanical ventilation (p=0.001), and develop COVID-19 complications such as ARDS and pneumonia (p=0.013 and p=0.09, respectively). Furthermore, patients with low or medium CT values were more likely to die compared to patients with high CT values (p=0.015). Multi-variant analysis showed that patients with low or medium CT values were more likely to have severe COVID-19 (p=0.041, p=0.039) in comparison to the patients with high CT values. The multi-variant analysis also showed a higher risk of mortality in patients with low CT values compared to patients with high CT values, although that was not significant (p=0.09).

Conclusion: Our findings revealed that CT values were an independent predictor of COVID-19 severity. The risk of mortality was higher in patients with low CT values. However, further investigation is needed to address the correlation between CT values and inflammatory factors.

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Reporting Complete Heart Block in a Patient with Polyarteritis Nodosa After COVID-19 Vaccination

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Keywords

Side effect; Atrioventricular block; Autoimmune disease; SARS-Cov-2

Abstract

Complete heart block (CHB) is a serious health condition, and polyarteritis nodosa (PAN) is an important autoimmune disease. During the COVID-19 pandemic, several vaccines were developed for the COVID-19 disease that showed several side effects, and some of these complications are still unknown. This is the first report of CHB in a patient with a history of PAN after COVID-19 vaccination. A 68-year-old man with a history of PAN was referred to our hospital, complaining of presyncope episodes and dizziness after receiving a COVID-19 vaccine. Physical examination, laboratory tests, and transthoracic echocardiography were normal. In his electrocardiogram, a narrow QRS complex, AV dissociation, and junctional escape rhythm were seen. Coronary angiography showed mild coronary artery disease. The patient, suffering from PAN for years, was hypothesized due to a few days after COVID-19 vaccination. This case report suggests that COVID-19 vaccines may interrupt the conduction system of the heart and the fact that underlying PAN may predispose to CHB following COVID-19 vaccination. Further studies are needed to accurately assess a possible association between PAN, CHB, and COVID-19 vaccines.

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High expression of MMP-2, MMP-9, ACE2, and TMPRSS2 in PBMC of patients with a severe type ofCOVID-19

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Keywords

TMPRSS2, ACE2, Lymphopenia, COVID-19

Abstract

Introduction: the symptoms and evidence of the response of peripheral blood mononuclear (PBMC) cells in patients with coronavirus have been shown in blood samples, which has raised concerns about the severe type and cytokine response in these patients. the purpose of this study is to determine whether the cell's PBMC surface possesses key factors required for cellular susceptibility to SARS-CoV-2 entry/infection.

Materials and Methods: This study included 88 individuals with mild (n=44) and severe (n=44)COVID-19, aged 36 to 60. an RT-qPCR experiment was used to analyze and evaluate the gene expression of the angiotensin-converting enzyme 2 (ACE2), trans-membrane protease serine 2 (TMPRSS2), metalloproteinases-2 (MMP-2), and metalloproteinases-2 (MMP-9) in different groups.

Results: the findings showed that patients with severeCOVID-19 had significantly higher gene expression of ACE2, TMPRSS2, MMP-2, and MMP-9 levels than those with mildCOVID-19.

Conclusions: Together, these Results suggest that PBMC cells surface in the immune system are susceptible to infection by SARS-CoV-2 and could therefore serve as a portal of entry as well as create a severe type of coronavirus of this virus. This highlights the importance of this gene pattern in creating a severe type of coronavirus of this virus.

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Differentially Expressed Inflammatory Cell Death-Related Genes And Serum Il-6 Levels Are Determinants for Severity of COVID-19

Authors

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Keywords

COVID-19, lymphopenia, apoptosis, pyroptosis, necroptosis, IL-6

Abstract

Introduction: the decrease in the lymphocyte percentage is a hallmark of COVID-19 that associates with a poor prognosis of the disease. Inflammatory cells death, PANoptosis (apoptosis, necroptosis, and pyroptosis), has been suggested to orchestrate the lymphocyte decrement among COVID-19 patients. the present study investigates the differences in the expression of key genes–related to inflammatory cell death as well as serum levels of IL-6 among mild and severeCOVID-19 patients with their correlation with lymphopenia.

Materials and Methods: Eighty-eight patients aged 36 to 60 years with mild (n=44) and severe (n=44) COVID-19 were enrolled in this study. The expression of key genes related to apoptosis (FADD), pyroptosis (ASC), and necroptosis (MLKL) genes was examined by RT-qPCR assay and compared between groups. The serum level of IL-6 was measured by the ELISA technique. The correlation between expression levels of subjected genes and serum levels of IL-6 with lymphopenia was also examined for mild and severe COVID-19 patients.

Results: The results revealed a significant increase in the expression of apoptosis (FADD), pyroptosis (ASC), and necroptosis (MLKL)-related genes among severe COVID-19 patients compared to patients with mild COVID-19. The serum levels of IL-6 also exhibited a significant increase among severe COVID-19 cases. Strikingly, a statistically significant negative correlation was detected between FADD, ASC, and MLKL expression and serum levels of IL-6 with the lymphocyte counts among severe and non-severe.

Conclusion: Our findings indicate that the main regulated cell-death pathways of apoptosis, necroptosis, and pyroptosis are likely to be involved in lymphopenia among COVID-19 patients, and the expression levels of these genes could potentially predict patients' outcomes. However, further research is warranted to examine their expression at the protein level.

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Quercetin And T Cells in Multiple Sclerosis Patients

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Keywords

Quercetin, Quercetin Penta Acetate, Prednisolone, Multiple sclerosis, Th17 cells.

Abstract

Introduction: the function of Th17 cells in the neuroinflammatory process in multiple sclerosis has been clarified. The production of IL-17 is dependent on the gene expression of RORc. It has been suggested that Quercetin can influence MS due to a variety of anti-inflammatory effects. Acetylation can enhance lipophilia, which is an important feature across the Blood-Brain-Barrier, so Quercetin Penta Acetate may cause more improvement for patients. the aim of the present study was to examine in vitro immunomodulatory aspect of Quercetin Penta Acetate as a modified compound on Th17 cells of MS patients, also compared with Quercetin and Methyl Prednisolone Acetate.

Materials and Methods: In the present *experimental* study, PBMCs were isolated and stained CFSE. Then, IC50 values were determined using different doses and times for Quercetin Penta Acetate and Methyl Prednisolone Acetate. Th17 cells proliferation by flow cytometry and gene expression of IL-17 and RORc by real-time PCR method were analyzed.

Results: The results showed that IL-17A gene expression was inhibited by Quercetin Penta Acetate (P = 0.0081), but Quercetin Penta Acetate did not have a significant inhibitory effect on Th17 cells proliferation (P= 0.59) and RORc gene expression (P =0.1), which was like Quercetin.

Conclusion: Taken together, our results showed some immunomodulatory aspects of Quercetin Penta Acetate on Th17 cells is more effective than Quercetin, and it might be considered to control some diseases such as MS as a compound by the natural base.

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Recombinant CD137-Fc, its synthesis, and applications to reduce the inflammation due to the novel coronavirus

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KEYWORDS

Autoimmune disorders, cancer immunotherapy, coronavirus inflammation, recombinant protein CD137-Fc, sCD137

Abstract

Introduction: CD137 (ILA/4-1BB), a member of tumor necrosis factor receptor superfamily, is one of the most important T cell costimulatory molecules. Interaction of this molecule with its ligand transmits a two-way signal that activates both T lymphocyte and antigen presenting cells. The soluble form of CD137 (sCD137) reduces the activity of its membrane isoform and is associated with T lymphocyte activation induced cell death. Recombinant CD137-Fc may be used to treat cancers, autoimmune disorders and viral infections. It may also be useful for management of coronavirus infection.

Materials and Methods: The 1276 bp DNA sequence encoded CD137-Fc recombinant protein was prepared and subcloned into lentiviral vector and expressed in transduced CHO-K1 eukaryotic cells. Western blot analysis, and enzyme-linked immuno sorbent assay tests were performed. The IL-6 and IL-8 levels as inflammatory cytokines were measured using the ELISA kits.

Results: Different assays results demonstrated that the expression of the 70-kDa CD137-Fc molecule was detectable without any degradation. IL-6 and IL-8 decreased significantly in the sample exposed to CD137-Fc protein.

Conclusion: This study helps to confirm previous research suggesting the use of this recombinant protein as a promising solution for the treatment of virus infections. This product is widely used in novel medical treatments, including cell-based immunotherapy such as dendritic cell, CAR T and CAR NK therapy. This product also is useful in the treatment of the 2019 coronavirus disease pandemic Because of its effect on reducing cytokine-induced inflammation.