Annals of
Clinical Epidemiology and Toxicology

Harfouch RM. Ann Clin Epi Toxi: ACET-105

Research Article Open Access

Multiple Organs Failure in COVID-19 Patients

Rim M. Harfouch*

Department of Microbiology, faculty of pharmacy, Al-Sham private university (ASPU), Latakia, Syria.

Abstract

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) in December 2019 form Wuhan, China leads to coronavirus disease 2019 (COVID-19) pandemic. COVID-19 is accompanied by multi-organ failure in severe patients. The involvement of different organs in severe patients results in lengthening the hospitalization duration and increasing the mortality rate. The multi-organ dysfunction is characterized by acute lung failure, acute liver failure, acute kidney injury, cardiovascular disease, and as well as a wide spectrum of hematological abnormalities and neurological disorders. The most important mechanisms are related to the direct and indirect pathogenic features of SARS-CoV2. Although the presence of angiotensin-converting enzyme 2, a receptor of SARS-CoV2 in the lung, heart, kidney, testis, liver, lymphocytes, and nervous system was confirmed, there are controversial findings to about the observation of SARS-CoV2 RNA in these organs. Moreover, the organ failure may be induced by the cytokine storm, a result of increased levels of inflammatory mediators, endothelial dysfunction, coagulation abnormalities, and infiltration of inflammatory cells into the organs. Therefore, further investigations are needed to detect the exact mechanisms of pathogenesis. Since the involvement of several organs in COVID-19 patients is important for clinicians, increasing their knowledge may help to improve the outcomes and decrease the rate of mortality and morbidity.

Keywords: *Multi-organ failure, coronavirus SARS-CoV-2, Characteristics.*

Introduction

The coronavirus SARS-CoV-2 has infected more than 250 million people and caused death to over than 5 million, with a worldwide mortality rate of 2%. Many patients who die from COVID-19 suffer from hyper-inflammation caused by cytokine storm syndrome (CSS) and associated acute respiratory distress syndrome [1]. The antiviral Remdesivir was shown to reduce the length of hospital stay for COVID-19 patients, but anti-inflammatory agents have improved survival in these patients [2]. The greatest survival rate has been found with glucocorticoids, which play as immunosuppressive agents, when given to patients with an oxygen requirement. However, patients treated with glucocorticoids may fare worse than those who receive standard care in the absence of an oxygen requirement or systemic inflammation. The selection of patients and timing of glucocorticoids administration is critical for survival benefit. Optimal treatment of targeted anti-cytokine therapy to prevent CSS is suggested earlier without increasing viral replication [3].

Definition of Cytokine storm syndrome (CSS)

Cytokine storm syndrome (CSS) is characterized by secretion of large amounts of cytokines including IL-1α, IL-1β, IL-6, IL-18 and TNF-α, continuous activation of lymphocytes and macrophages causing immune dysregulation, and finally, overwhelming systemic inflammation and multi-organ failure (MOF) with high mortality [4].

The term CSS was first used after allogeneic stem cell transplant to describe the hypercytokinemia (increased blood cytokines) in graft. Many viral, bacterial and parasitic infections can cause CSS such as Mycobacterium tuberculosis and Epstein-Barr virus (EBV), which cause pathological immune activation characterized by elevated cytokines such as interferon-γ (IFN-γ) in patients with immune defects [5].

Levels of inflammatory cytokines especially IL-6, IL-8, MCP-1 and TNFα are significantly increased in COVID-19 plasma. Plasma levels of IL-8 are strongly associated with circulating vWF levels. Local and systemic circulating inflammatory markers concur with several markers revealing endothelial activation and damage in COVID-19 patients.

Pathogenesis of CSS

The pathogenesis of CSS has not been fully known. Several studies have shown that the mechanism of CSS depends on the imbalance of pro-inflammatory and anti-inflammatory process and the interaction of specific cells and cytokines, resulting in immune regulation disorder. Cytokines can be markedly increased in patients with CSS, which differ according to the heterogeneity of the disease. A previous study found that H5N1 infected patients had higher levels of interferon-gamma-induced protein-10 (IP-10), monocyte chemoattractant protein 1 (MCP-1) and IL-8 than patients with seasonal H1N1 influenza [6]. Moreover, it was

***Corresponding author:** Rim M. Harfouch, Department of Microbiology, faculty of pharmacy, Al-Sham private university (ASPU), Latakia, Syria. Email: r.h.foph.lat@aspu.edu.sy*

***Citation:** Harfouch RM (2022) Multiple Organs Failure in COVID-19 Patients. Ann Clin Epi Toxi: ACET-105.*

***Received Date:** August 01, 2022; **Accepted Date:** August 06, 2022; **Accepted Date:** August 10, 2022*

***Copyright:** © 2022 Harfouch RM. This is an open-access article distributed under the terms of the Creative Commons attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.*

confirmed that cytokines play an important role in the pathogenesis of severe CoV infection. The proinflammatory cytokines (IFN-γ, IL-1, IL-6, IL-12, transforming growth factor-β (TGF-β)) in severe SARS patients' sera were significantly higher than those with mild to moderate symptoms. Also, in severe MERS patients, serum inflammatory cytokines (IFN-α, IL-6, IL-8) were significantly increased [7].

Mechanisms of CSS in COVID-19

The cytokine storm in COVID-19 may vary from the cytokine storms in other clinical settings. It was revealed by autopsy findings, that the lymphoid tissues were destroyed in COVID-19 patients, which is rare from CSS in sepsis and CAR T-cell therapy. Spleen and lymph node atrophy are observed in patients with COVID-19, while lymphadenopathy and splenomegaly are more common in other CSS-related diseases. However, the specific mechanisms for these differences remain unclear and need to be further studied [8].

Coronaviruses (CoVs) are enveloped single-stranded RNA viruses, which have caused two marked pandemics SARS and MERS [9]. Spike (S) proteins of coronaviruses, including the SARS-CoV, facilitate entry into their target cells via the interaction with angiotensin-converting enzyme 2 (ACE2), a functional cellular receptor, which is highly expressed in vascular endothelial cells, alveolar epithelial cells, intestinal epithelial cells and renal proximal tubular cells. ACE2 suppresses angiotensin II(AngII) and activates the formation of angiotensin 1–7, a which is a vasodilator heptapeptide. The binding of the coronavirus spike protein to ACE2 leads to the down-regulation of ACE2, which in turn results in excessive production of vasoconstrictor AngII and reduced production of vasodilator angiotensin 1–7.

Furthermore, AngII binds to the angiotensin receptor 1 (AT1R) and plays a role of proinflammatory cytokine. The AngII-AT1R axis activates NF-κB and metalloprotease 17 (ADAM17), which stimulates the production of the epidermal growth factor receptor (EGFR) ligands and TNF-α, which activate the IL-6 amplifier (IL-6 Amp), and lead to a hyperinflammatory status, resulting in increased vascular permeability of the lungs [10].

A retrospective study also found higher plasma concentrations of IL-2, IL-7, IL-10, IP-10, MCP-1, and TNF-α in intensive care unit (ICU) patients compared with nonsevere patients, suggesting a cytokine storm in severe patients [11].

Diagnosis of CSS in COVID-19

There is no standard for the diagnosis of CSS related to COVID-19, so further clinical and laboratory investigations are needed. The basic principles for consideration of CSS in COVID-19 are the following presentations:

1. A rapid or sudden regression of multiple organ functions (cardiac, liver or renal injury).
2. The elevation of systematic inflammatory biomarkers (such as CRP, erythrocyte sedimentation rate and serum ferritin).
3. A significant decrease of lymphocyte counts.
4. The elevation of cytokines, such as IL-1β, IL-2R, IL-6, IP-10, MCP-1, TNF-α and IFN-γ.

Clinicians should keep highly alert on the possibility of CSS under these circumstances. However, that CSS is highly heterogeneous and may present with unspecific syndromes, the diagnosis of CSS in COVID-19 is very challenging and the development of a specific diagnostic test that helps to make the diagnosis of CSS earlier is a high priority for future research [12].

The inflammatory disorders in COVID-19 have been reported in many studies. COVID-19 causes a decrease of lymphocyte count and an increase of C reactive protein (CRP), especially in severely ill patients. The major subtypes of T lymphocytes (T cell) (CD3+ CD4+ T cell and CD3+ CD8+ T cells) are reduced in the COVID-19 and are significantly lower in the severe cases. Other immune cells, B cell and natural killer (NK) cell, have more inconsistency in recent studies [13].

Conclusion

The clinical, immunological, and pathologic features of COVID-19 have something in common with SARS and MERS. All the viruses can cause lymphopenia and influenza-like symptoms in the early stage. SARS and COVID-19 do not lead to the elevation of TNF-α, but the increase of IL-6 and IL-10 is more common in COVID-19. The IL-6 plays a crucial role in the pathologic of COVID-19, including the chemotaxis of neutrophils and lymphocyte necrosis. Importantly, COVID-19 is more able to cause cytotoxic lymphocytes exhaustion.

References

1. Harfouch RM, Moualla YM, Shahoud SM, Belal LA, Mohammad BS, Mustafa NM, Souliman OA, Elshemali YI (2021). Epidemiology of COVID-19 in the most pandemic Countries: A review article. Acad. J. Biotechnol. 9(1): 021-027.
2. Rim M. Harfouch, Samer Alshaikh, Mohammad Alshimaly, Amany Assaad, Jehan Ahmad, Haya Zoughaibi, Maher Hammadi, Yahya Elshimali. Therapeutic approaches for COVID 19: Challenges and successes. Ann Clin Anal Med 2020; DOI: 10.4328/ACAM.202
3. Cron, R.Q., Caricchio, R. & Chatham, W.W. Calming the cytokine storm in COVID-19. Nat Med 27, 1674–1675 (2021). https://doi.org/10.1038/s41591-021-01500-9.
4. Shimizu M. Clinical Features of Cytokine Storm Syndrome. In: Cron RQ, Behrens EM, eds. Cytokine Storm Syndrome. Cham, Springer International Publishing, 2019; pp. 31–41.
5. Chen LYC, Hoiland RL, Stukas S, Wellington CL, Sekhon MS. Confronting the controversy: interleukin-6 and the COVID-19 cytokine storm syndrome. Eur Respir J. 2020;56(4):2003006. Published 2020 Oct 1. doi:10.1183/13993003.03006-2020
6. Harfouch RM. Cytokine Storm Syndrome in Covid-19 Patients: Characteristics and Diagnosis. Journal of Clinical Epidemiology & Toxicology. SRC/JCET-131. DOI: doi. org/10.47363/JCET/2021 (2). 2021;121:2-3.
7. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017; 39: 529– 39.

8. Yao XH, Li TY et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. Chin. J. Pathol 2020; 49: E009.
9. Alhouri A, Salloum A, Harfouch RM, Soumya G. Possible Side Effects of using Detergents during the Covid19 Pandemic in Syria. Ann Clin Cases. 2020;1(4):1023.
10. Murakami M, Kamimura D, Hirano T. Pleiotropy and specificity: insights from the interleukin 6 family of cytokines. Immunity 2019; 50: 812–31.
11. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497–506.
12. Harfouch RM (2022) Antiviral Effects of Propolis against SARS-COV 2. Int J Clin Med Imaging 9:809.
13. Tang Y, Liu J, Zhang D, Xu Z, Ji J and Wen C (2020) Cytokine Storm in COVID-19: The Current Evidence and Treatment Strategies. Front. Immunol. 11:1708. doi: 10.3389/fimmu.2020.01708