International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijarbs Coden: IJARQG (USA) Volume 10, Issue 3 -2023

Review Article

DOI: http://dx.doi.org/10.22192/ijarbs.2023.10.03.020

An update on cytokine storm in covid-19 infection: Pivotal to the survival of the patients

*Emmanuel Ifeanyi Obeagu[1], Swalehe Hamisi[1] and Umi Omar Bunu[2]
[1]Department of Medical Laboratory Science, Kampala International University, Uganda
[2]Department of Public Health, Kampala International University, Uganda.
Email: *emmanuelobeagu@yahoo.com*

Abstract

The immune system protects the host organism from exogenous and endogenouspathogens. A finely tuned and balanced array of cytokines, coagulation factors, andcomplement together with immunocompetent cells protect the body from a wide variety ofknown and unknown invaders. Usually, pro- and anti-inflammation are tightly regulatedto adequately counter the infectious event. A pro-inflammatory milieu typically dominatesthe initial phase; however, anti-inflammation is initiated early to reach a new equilibriumand to start tissue repair processes. Various pathogens and malignant and autoimmune diseases as well as genetic changes, but also iatrogenic interventions, can disturb this equilibrium so that an excessive release of cytokines can occur. In its severe (albeit rare) form, this is referred to as cytokine storm. As a result, positive feedback mechanisms and self-sustained activation of immune cells occur. The resulting hyperinflammation can lead to a life-threatening condition.

Keywords: cytokine storm, Covid-19, immunity, hyper-inflammation, immunocompetent

Introduction

Cytokinesare a broad and loose category of small proteins important in cell signaling.cytokines are peptides and cannot cross the lipid bilayer of cells to enter the cytoplasm. Cytokine have been shown to be involved in autocrine, paracrine and endocrine signaling as immunomodulating agent (Wenjun *et al.*, 2020).

Various pathogens, autoimmune and malignant diseases, but also genetic disordersand certain therapeutic interventions, can lead to life-threatening systemic inflammatory syndromes in the human body (Breslin, 2007).

Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly spread worldwide and was declared a pandemic in early 2020. COVID-19 destroyed people's mental and physical health and staggered global economic growth. As of May 18, 2021, 163 million infections, including 3.38 million deaths, have been recorded. SARS-CoV-2

invades the host by virtue of angiotensin-converting enzyme 2 (ACE2) receptors broadly distributed on various tissues and immune cells (Ni *et al*., 2020).

The virus can cause a wide range of clinical manifestations from mild forms such as fever, cough, and myalgia to moderate forms requiring hospitalization (pneumonia and localized inflammation) to severe/critical forms with fatal outcomes(Shen *et al*., 2021).

Severe or critical infection often manifests as pneumonia,disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS), low blood pressure, and multiorgan failure(Obeagu *et al.,* 2021; Asogwa *et al.,* 2021; Hassan *et al.,* 2022; Obeagu *et al.,* 2021; Obeagu, 2022; Nnodim *et al.,* 2022).Several lines of evidence have shown that immunopathological damage may be responsible for the deterioration of COVID-19 (Anka e*t al*., 2021).

Particularly, multiple studies have reported that highly elevated levels of pro-inflammatory cytokines are produced during the crosstalk between epithelial cells and immune cells in COVID-19(Okorie *et al.,* 2022; Obeagu and Babar, 2021; Obeagu *et al.,* 2023; Obeagu *et al.,* 2023), which has linked the cytokine storm (CS) with the severe complications and poor outcomes in this infection(Rabaan *et al.*, 2021).

CS is a fast-developing, life-threatening, clinical condition in which the overproduction of inflammatory cytokines and excessive activation of immune cells lead to complicated medical syndromes from a persistent fever, nonspecific muscle pain, and hypotension, to capillary leak syndrome, DIC, ARDS, hemophagocyticlymphohistiocytosis (HLH), multi-organ failure, and death if treatment is not adequate (Buicu e*t al.*, 2021).

Therefore, the timing of diagnosis and treatment of CS could be life-saving. The term CS was first used in 1993 in graft-versus-host disease,and later, in many inflammatory diseases such as autoimmune conditions, organ transplantation, cancer chimeric antigen receptor (CAR) T cell therapy, and, most recently, in COVID-19. However, the profile and causative effect of CS in different conditions can greatly vary. Thus far, precise diagnosis and treatment guidelines for CS in most of the conditions are lacking. Understanding the definite alterations and pathogenic roles of individual cytokines involved in the COVID-19-related CS (COVID-CS) is hence extremely important for the development of precise diagnosis and effective treatment (Zhang *et al*., 2020).

A cytokine storm in COVID-19

Also called hypercytokinemia,is a physiological reaction in humans and other animals in which the innate immune system causes an uncontrolled and excessive release of pro inflammatory signaling molecules called cytokines. Normally, cytokines are part of the body's immune response to infection, but their sudden release in large quantities can cause multisystem organ failure and death (Fajgenbaum and June, 2020).Cytokine storms can be caused by a number of infectious and non-infectious etiologies, especially viral respiratory infections such as H1N1 influenza, H5N1 influenza, SARS-CoV-1, and SARS-CoV-2, Influenza B, Parainfluenza virus. Other causative agents include the Epstein-Barr virus, cytomegalovirus, group A streptococcus, and non-infectious conditions such as graft-versus-host disease.The viruses can invade lung epithelial cells and alveolar macrophages to produce viral nucleic acid, which stimulates the infected cells to release cytokines and chemokines, activating macrophages, dendritic cells, and others (*Thepmankorn et al.,* 2021).

Cytokine storm syndrome is a diverse set of conditions that can result in a cytokine storm. Cytokine storm syndromes include familial hemophagocyticlymphohistiocytosis, Epstein-Barr virus–associated hemophagocytic, lymphohistiocytosis, systemic or non-systemic juvenile idiopathic arthritis–associated

macrophage activation syndrome, NLRC4 macrophageactivation syndrome, cytokine release syndrome and sepsis(Hafezi *et al.*, 2021).The cytokine storm evolved from the earliest forms as intracellular molecules before the appearance of receptor and signaling cascades. Cytokine like activities has been demonstrated in invertebrates such as star fish and Drosophilia, where they played as essential role in host defense and repair (Jahandideh *et al.*, 2020).In COVID-19 can trigger a cytokine storm in pulmonary tissue through hyperactivation of the immune system and the uncontrolled release of cytokine (Heydarian *et al*., 2022) .The trigger cytokines storm is an uncontrolled immune response resulting in continuous activation and expansion of immune cells,lymphocyte and macrophages which produce immense amount of cytokine which result into cytokine storm.

Cytokine storm is cause by the colossal release of proinflammatory cytokines example IL(interleukin)-2,IL-6,IL-8 TNF(tumor necrotic factor)-α,) causing dysregulated, hyperimmune response. This immune pathogenesis lead to acute lung injury and acute respiratory distress syndrome(ARDS) (Xiao *et al.*, 2020).Targeting cytokine storm with the therapies that are already available in India with the support of published guidelines and consensus can assist in achieving a better outcome in Covid-19.

Cytokine storm

The first reference to the term cytokine storm in the published medical literature appears to be by James Ferrara in 1993 during a discussion of graft vs. host disease, a condition in which the role of excessive and self-perpetuating cytokine release had already been under discussion for many years (Ferrara, *1993*).It is believed that cytokine storms were responsible for the disproportionate number of healthy young adult deaths during the 1918 influenza pandemic, which killed an estimated 50 million people worldwide. In this case, a healthy immune system may have been a liability rather than an asset(*Taubenberger* and Morens, 2020).Preliminary research results from Taiwan also indicated this as the probable reason for many deaths during the SARS epidemic in 2003. Human deaths from the bird flu H5N1 usually involve cytokine storms as well(Shrestha *et al*., 2021).Cytokine storm has also been implicated in hantavirus pulmonary syndrome(Vadell *et al*., 2019).

In 2006, a study at Northwick Park Hospital in England resulted in all 6 of the volunteers given the drug theralizumab becoming critically ill, with multiple organ failure, high fever, and a systemic inflammatory response. Parexel, a company conducting trials for pharmaceutical companies claimed that theralizumab could cause a cytokine storm—the dangerous reaction the men experienced.

Common biomarkers affected during cytokine storm in COVID-19

Mediator (Abbreviation) Cytokines	Main Source	Major Function
IL-1	macrophages, pyroptotic cells, epithelial cells	Proinflammatory; pyrogenic function; activation of macrophage and TH17 cells
IL-2	T cells	Immune response; Teff and Tregcell growth factor; T-cell differentiation
IL-4	TH2 cells, basophils, eosinophils, mast cells, NK cells.	Anti-inflammatory; TH2 differentiation;adhesion; chemotaxis.
IL-6	T cells, macrophages,	Proinflammatory; pleiotropic;

	endothelial cells	pyrogenic function; acute phase response; lymphoid differentiation; increased antibodyproduction.
IL-9	TH9 cells	Pleiotropic; stimulation of B, T, and NK cells; protection from helminthesinfections; activation of mast cells; association with type I interferon in COVID-19.
IL-10	regulatory T cells, TH9 cells.	Anti-inflammatory; inhibition of macrophage activation; inhibition of TH1 cells and cytokine release.
IL-12	dendritic cells, macrophages	Stimulation of T and NK cells; activation of TH1 pathway; induction of interferon- from TH1 cells; cytotoxic T cells and NK cells; acting in synergy with interleukin-18
IL-13	TH2 cells	Anti-inflammatory; differentiation of B cells; mediator of humoral immunity

(Fanelli et *al*., 2020).

Pathophysiology of cytokine storm in Covid-19 patients

Inflammation is the mechanism that multicellular organisms have evolved to defeatinvasive pathogens and initiate healing of injured tissue. A balanced, “protective” inflammatoryresponse consists of diverse mechanisms and involves activation of both pro- and anti-inflammatory pathways within the innate and the acquired immune systems. The immune system can recognize and counteract previously unknown pathogens by initiating different defensive pathways. After successful defense and initiation of healing, the immune system returns to a state of homeostasis and assumes a wait-and-see role. All of this is achieved by complex mechanisms that are controlled and balanced by multiple activating and inhibitory feedback loops. Cytokines play a pivotal role in these control mechanisms by regulating the immune response, which they can, thus, amplify but also dissolve. By default, their comparatively short biological half-lives prevent remote effects outside the inflammatory foci. In thecase of disseminated infections, increased levels of circulating cytokines may also occur although this is generally considered pathological. However, it is precisely this systemic effect that can lead to collateral damage to various vital organ systems. Numerous proandanti-inflammatory factors are involved in the context of a dysregulated inflammatory response, as occurs in CS. In addition to cytokines and factors of the complement and coagulation systems, cellular responses—mediated by, e.g., monocytes, macrophages, neutrophils, NK cells, and endothelial cells—also play a role(*Aslani et al*., 2021).

Example of signal pathway of cytokine storm for COVID -19

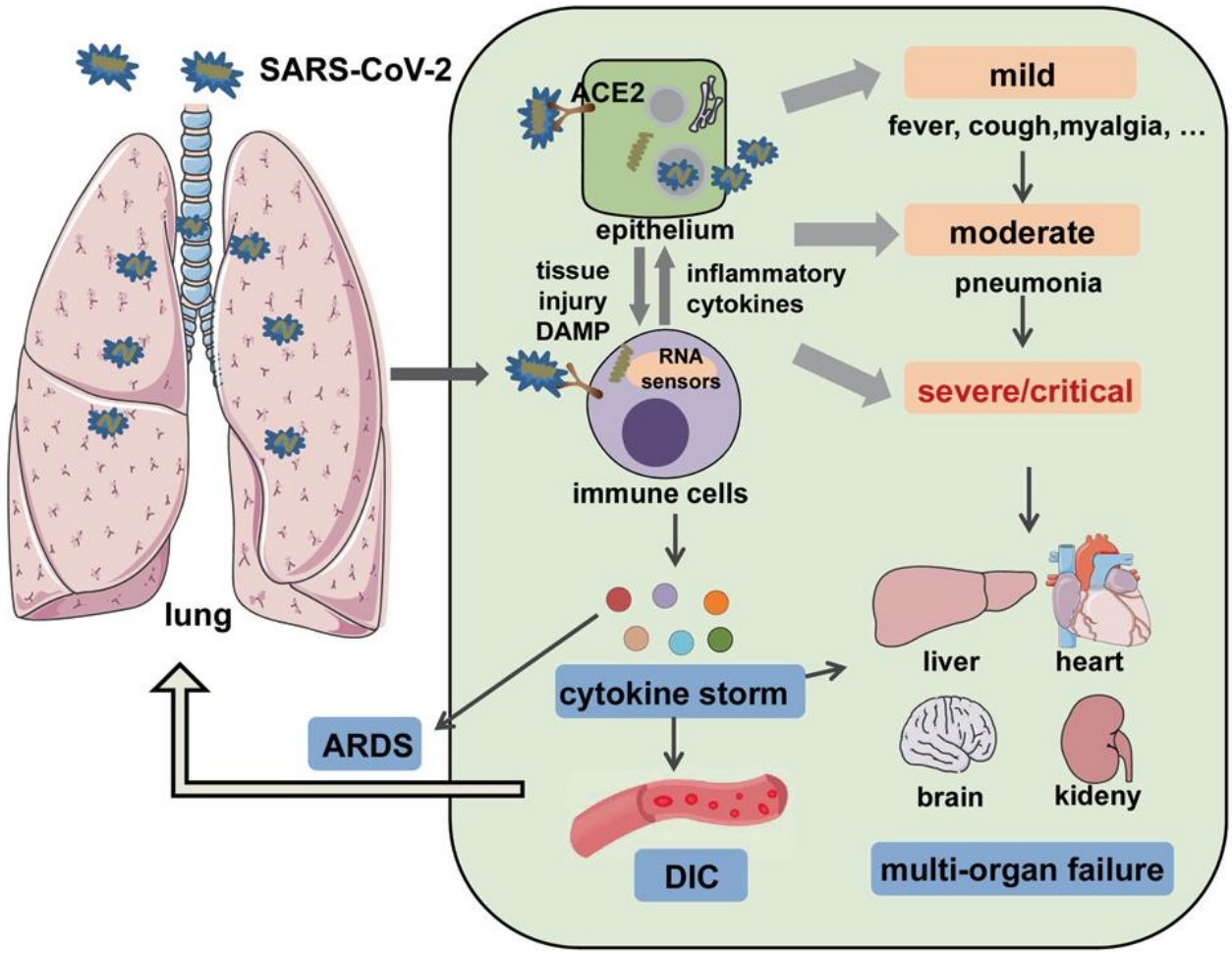

Fig. 1 A systemic clinical manifestations of COVID-19. SARS-CoV-2 infects airway epithelial cells or immune cells via binding to ACE2 receptors, causing tissue damage and release of DAMPs, as well as production of inflammatory cytokines by epithelial cells and immune cells. Then, the crosstalk between epithelial cells and immune cells leads to a wide range of clinical manifestations, from mild forms (e.g., fever, cough, and myalgia); to moderate forms requiring hospitalization (pneumonia and localized inflammation); to severe/critical forms with a fatal outcome that are manifested as pneumonia, ARDS, DIC, CS, and multiorgan failure. DAMP danger associated molecular pattern, ARDS acute respiratory distress syndrome, DIC disseminated intravascular coagulation (Yang *etal*., 2021).

Viral and Parasitic Infections

Infection with certain viral pathogens is frequently accompanied by an excessive release of cytokines. These include MERS-CoV, influenza virus, and haemorrhagic fevers. Different viruses are associated with diverse patterns of cytokine release, but so far, this hasnot been operationalized in terms of a comprehensive and universally effective therapeutic approach (Vecchié et *al*., 2021).

Parasitic infections are also associated with the development of CS; there are corresponding reports for infection with plasmodium falciparum and visceral leishmaniasis, among others. In research on Malawian children with different manifestations of malaria, it could be shown that the simultaneous occurrence of

high levels of pro- and anti-inflammatory cytokines could contribute to the pathogenesis of cerebral malaria (*Mandalaetal.*, 2017).

Viral- vs. Non-Viral-Induced Cytokine Storm

The clinical picture of infective systemic inflammation is uniform, regardless of whether there is an underlying bacterial or viral cause. Even non-specific, non-infectious inflammation such as trauma or allergic reactions present with symptoms such as fever, increased respiratory rate, and tachycardia. he endogenous processes of host defense in bacterial and viral infections differ in several aspects (*Madeddu*, 2020). The immune response to infection by bacteria is initially fundamentally different from that to viruses: In simple terms, the innate immune system recognizes and destroys bacteria, which are mostly extracellular, with the help of the classical and alternative complement pathway and phagocytosis, among other mechanisms. Viruses, on the other hand, replicate intracellularly and infected cells are recognized and destroyed largely by the adaptive immune system. In this process, cytotoxic T cells, which recognize viral epitopes presented by MHC-I molecules, antibodies, and interferons play key roles. The development of CS from the various underlying basic mechanisms is a multifactorial process with numerous variables, some of which will be discussed here as examples.

Clinical symptom of cytokine storm in Covid - 19 patients

The cytokine storm symptoms are varied and might include

- Fevers and chills
- Fatigue
- Swelling of extremities
- Nausea and vomiting
- Muscle and joint aches
- Headache
- Rashes
- Cough
- Shortness of breath
- Rapid breath
- Seizures
- Difficult coordinating movement
- Confusion and hallucination
- Lethargy and poor responsiveness (Sun et *al.*, 2020)

Cytokine storm diagnosis in Covid-19 patients

The underlying medical condition when diagnosing cytokine storm, a person might need to be diagnosed with

- A genetic disorder
- An autoimmune condition
- An infectious disease, like Covid-19,

Depending on the situation, this might require various kinds of medical tests, medical history and a physical examination provide diagnostic points. This is important because cytokine storm can affect so many different systems of the body. Also Laboratory abnormalities, may be seen in basic blood tests, can provide clues. People with cytokine storm might have abnormalities

- Decrease number of immune cells?
- Elevation in markers of kidney or liver damage like (ALT &AST)
- Elevation in inflammatory marker like c-reactive protein (CRP)
- Abnormalities in markers of blood clotting(Marin Oyarzún and Heller, 2019)
- Elevated ferritin(involved in infection response)(Para et *al*., 2022)

Cytokine storm treatment in Covid-19 patients

Supportive care is a critical part of the treatment for cytokine storm. Sometimes an individual is experiencing severe symptoms like difficulty in breathing. They may need care in an intensive care unit. This might include support as follows

- Intensive monitoring of vital signs
- Ventilation support
- Fluid given intravenously

- Management of electrolyte
- Hemodialysis

In some situations, it may be possible to treat the underlying source of the cytokine storm. Example if cytokine storm is caused by bacteria infections the antibiotics may be helpful(Yang et *al*., 2021).

Conclusion

The cytokine storm in Covid -19 leads to deleterious clinical manifestations or even acute mortality in critically ill patients with Covid D-19. Likewise may cause a damage of organs and also Impaired acquired immune responses and uncontrolled inflammatory innate responses may be associated with the mechanism of the cytokine storm. Early control of the cytokine storm through therapies, such as immunomodulators and cytokine antagonists, is essential to improve the survival rate of the patients.

References

Anka, A. U., Tahir, M. I., Abubakar, S. D., Alsabbagh, M., Zian, Z., Hamedifar, H., Sabzevari, A. and Azizi, G. (2021). Coronavirus disease 2019 (COVID-19): An overview of the immunopathology, serological diagnosis and management. In *Scandinavian Journal of Immunology*. https://doi.org/10.1111/sji.12998

Aslani, M., Mortazavi-Jahromi, S. S. and Mirshafiey, A. (2021). Cytokine storm in the pathophysiology of COVID-19: Possible functional disturbances of miRNAs. In *International Immunopharmacology*. https://doi.org/10.1016/j.intimp.2021.108172

Breslin, S. (2007). Cytokine-release syndrome: overview and nursing implications. In *Clinical journal of oncology nursing*. https://doi.org/10.1188/07.cjon.s1.37-42

Buicu, A. L., Cernea, S., Benedek, I., Buicu, C. F., & Benedek, T. (2021). Systemic inflammation and COVID-19 mortality in patients with major noncommunicable diseases: Chronic coronary syndromes, diabetes and obesity. In *Journal of Clinical Medicine*. https://doi.org/10.3390/jcm10081545

Fajgenbaum, D. C. and June, C. H. (2020). Cytokine Storm. *New England Journal of Medicine*. https://doi.org/10.1056/nejmra2026131

Fanelli, V., Montrucchio, G., Sales, G., Simonetti, U., Bonetto, C., Filippini, C., Mengozzi, G., Urbino, R., Cappello, P. and Brazzi, L. (2020). Immune Response Profile of SARS-CoV-2 Associated AARDS Patients During Extracorporeal Membrane Oxygenation. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.3624462

Ferrara, J. L. M. (1993). Cytokine dysregulation as a mechanism of graft versus host disease. *Current Opinion in Immunology*. https://doi.org/10.1016/0952-7915(93)90139-J

Hafezi, B., Chan, L., Knapp, J. P., Karimi, N., Alizadeh, K., Mehrani, Y., Bridle, B. W. and Karimi, K. (2021). Cytokine storm syndrome in sars-cov-2 infections: A functional role of mast cells. In *Cells*. https://doi.org/10.3390/cells10071761

Heydarian, M., Mohammadtaghizadeh, M., Shojaei, M., Babazadeh, M., Abbasian, S. and Amrovani, M. (2022). The effect of COVID-19 derived cytokine storm on cancer cells progression: double-edged sword. In *Molecular Biology Reports*. https://doi.org/10.1007/s11033-021-06800-4

Jahandideh, B., Derakhshani, M., Abbaszadeh, H., Akbar Movassaghpour, A., Mehdizadeh, A., Talebi, M. and Yousefi, M. (2020). The pro-Inflammatory cytokines effects on mobilization, self-renewal and differentiation of hematopoietic stem cells. In *Human Immunology*. https://doi.org/10.1016/j.humimm.2020.01.004

Madeddu, P. (2020). Cardiovascular complications of COVID-19: evidence, misconceptions, and new opportunities.

Vascular Biology. https://doi.org/10.1530/vb-20-0008

Mandala, W. L., Msefula, C. L., Gondwe, E. N., Drayson, M. T., Molyneux, M. E. and MacLennan, C. A. (2017). Cytokine profiles in Malawian children presenting with uncomplicated malaria, severe malarial anemia, and cerebral malaria. *Clinical and Vaccine Immunology*. https://doi.org/10.1128/CVI.00533-16

Marin Oyarzún, C. P. and Heller, P. G. (2019). Platelets as mediators of thromboinflammation in chronic myeloproliferative neoplasms. In *Frontiers in Immunology*. https://doi.org/10.3389/fimmu.2019.01373

Ni, W., Yang, X., Yang, D., Bao, J., Li, R., Xiao, Y., Hou, C., Wang, H., Liu, J., Yang, D., Xu, Y., Cao, Z. and Gao, Z. (2020). Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. In *Critical Care*. https://doi.org/10.1186/s13054-020-03120-0

Para, O., Caruso, L., Pestelli, G., Tangianu, F., Carrara, D., Maddaluni, L., Tamburello, A., Castelnovo, L., Fedi, G., Guidi, S., Pestelli, C., Pennella, B., Ciarambino, T., Nozzoli, C. and Dentali, F. (2022). Ferritin as prognostic marker in COVID-19: the FerVid study. *Postgraduate Medicine*. https://doi.org/10.1080/00325481.2021.1990091

Rabaan, A. A., Al-Ahmed, S. H., Muhammad, J., Khan, A., Sule, A. A., Tirupathi, R., Mutair, A. Al, Alhumaid, S., Al-Omari, A., Dhawan, M., Tiwari, R., Sharun, K., Mohapatra, R. K., Mitra, S., Bilal, M., Alyami, S. A., Emran, T. Bin, Moni, M. A. and Dhama, K. (2021). Role of inflammatory cytokines in covid-19 patients: A review on molecular mechanisms, immune functions, immunopathology and immunomodulatory drugs to counter cytokine storm. *Vaccines*. https://doi.org/10.3390/vaccines9050436

Shen, W. X., Luo, R. C., Wang, J. Q. and Chen, Z. S. (2021). Features of Cytokine Storm

Identified by Distinguishing Clinical Manifestations in COVID-19. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2021.671788

Shrestha, D., Bhattachan, B., Parajuli, H. and Shrestha, S. (2021). Avian/Bird flu: A review: H5N1 outbreaks in Nepal. *Nepal Journal of Biotechnology*. https://doi.org/10.3126/njb.v9i1.38647

Sun, X., Wang, T., Cai, D., Hu, Z., Chen, J., Liao, H., Zhi, L., Wei, H., Zhang, Z., Qiu, Y., Wang, J. and Wang, A. (2020). Cytokine storm intervention in the early stages of COVID-19 pneumonia. In *Cytokine and Growth Factor Reviews*. https://doi.org/10.1016/j.cytogfr.2020.04.002

Taubenberger, J. K. and Morens, D. M. (2020). The 1918 influenza pandemic and its legacy. *Cold Spring Harbor Perspectives in Medicine*. https://doi.org/10.1101/cshperspect.a038695

Thepmankorn, P., Bach, J., Lasfar, A., Zhao, X., Souayah, S., Chong, Z. Z. and Souayah, N. (2021). Cytokine storm induced by SARS-CoV-2 infection: The spectrum of its neurological manifestations. In *Cytokine*. https://doi.org/10.1016/j.cyto.2020.155404

Vadell, M. V., Carbajo, A. E., Massa, C., Cueto, G. R. and Gómez Villafañe, I. E. (2019). Hantavirus Pulmonary Syndrome Risk in Entre Ríos, Argentina. *EcoHealth*. https://doi.org/10.1007/s10393-019-01425-3

Vecchié, A., Bonaventura, A., Toldo, S., Dagna, L., Dinarello, C. A. and Abbate, A. (2021). IL-18 and infections: Is there a role for targeted therapies? In *Journal of Cellular Physiology*. https://doi.org/10.1002/jcp.30008

Wenjun, W., Xiaoqing, L., Sipei, W., Puyi, L., Liyan, H., Yimin, L., Linling, C., Sibei, C., Lingbo, N., Yongping, L. and Jianxing, H. (2020). The definition and risks of cytokine release syndrome-like in 11 COVID-19-infected pneumonia critically ill patients: Disease characteristics and retrospective analysis. *MedRxiv*.

Xiao, T., Yan, Z., Xiao, S. and Xia, Y. (2020). Proinflammatory cytokines regulate epidermal stem cells in wound epithelialization. In *Stem Cell Research and Therapy*. https://doi.org/10.1186/s13287-020-01755-y

Yang, L., Xie, X., Tu, Z., Fu, J., Xu, D. and Zhou, Y. (2021). The signal pathways and treatment of cytokine storm in COVID-19. In *Signal Transduction and Targeted Therapy*. https://doi.org/10.1038/s41392-021-00679-0

Zhang, S., Li, L., Shen, A., Chen, Y. and Qi, Z. (2020). Rational Use of Tocilizumab in the Treatment of Novel Coronavirus Pneumonia. In *Clinical Drug Investigation*. https://doi.org/10.1007/s40261-020-00917-3

Obeagu, E. I., Babar, Q., Vincent, C. C. N., Okafor, C. J., Eze, R., Chijioke, U. O., Ibekwe, A. M. and Uduchi, I. O. (2021). Pulmonary Embolism in Covid-19 Pandemic: A Threat to Recovery of the Infected Patients. *Journal of Pharmaceutical Research International*, 33(42A), pp. 90–98. doi: 10.9734/jpri/2021/v33i42A32388.

Asogwa, E.I., Obeagu, E.I., Abonyi, O.S., Elom, C.O., Akamike, I.C., Udeoji, D.U., Egbumike, C.J., Agunwah, E.U., Eze, C.N. and Esimai, B.N. (2021). Mitigatingthe Psychological Impacts of COVID-19in Southern Nigeria. Journal of Pharmaceutical Research International.; 33(30A): 72-83

Hassan, A. O., Obeagu, E. I., Ajayi, D. T., Tolulope, A. A., Madekwe, C. C., Madekwe, C. C., Ikpenwa, J. N. and Nakyeyune, S. (2022). COVID 19 Omicron: The Origin, Presentation, Diagnosis, Prevention and Control. Asian Journal of Research in Infectious Diseases, 11(1), 25-33.

Obeagu, E.I., Babar, Q., Vincent, C.C.N., Okafor, C.J., Eze, R., Chijioke, U.O., Ibekwe, A.M. and Uduchi, I.O. (2021). Pulmonary Embolism in Covid-19 Pandemic: A Threat to Recovery of the Infected Patients.. Pulmonary Embolism in Covid-19 Pandemic: A Threat to Recovery of the Infected Patients", Journal of Pharmaceutical Research International. 33(42A), pp. 90-98.

Obeagu, E.I. (2022). COVID 19: FactorsAssociated with Implementation and Practice of Covid-19Prevention. Int. J. Adv. Multidiscip. Res. 9(9): 37-42. DOI: http://dx.doi.org/10.22192/ijamr.2022.09.09.004

Nnodim, J., Njoku-Obi, T., Ohalete, C. and Obeagu, E. I. (2022). Perspective of Covid 19 Hesistancy. *Madonna University Journal of Medicine and Health Sciences ISSN: 2814-3035*, *2*(1), 235-238.

Okorie, N. Adeniran, O.C, Adimabua, O.P.,Obeagu, E.I. and Anastasia, E.e. (2022) *Pathological Changes among Norvegicus Rattus Exposed on Novel Smoked Bambusa Vulgaris (Bamboo) Leaf: Cigarette Substitute during COVID-19 Lockdown in Nigeria*. Journal of Advances in Medical and Pharmaceutical Sciences, 24 (7): 30-39.

Obeagu, E.I., and Babar, Q. (2021). Covid-19 and Sickle Cell Anemia: Susceptibility and Severity. J. Clinical and Laboratory Research. 3(5); DOI:10.31579/2768-0487/056

Obeagu, E.I., Scott, G.Y., Amekpor, F., Ugwu, O.P.C. and Alum, E.U. (2023). Covid-19 Infection and Diabetes: A Current Issue. *International Journal of Innovative and Applied Research*. **11** (1):25-30.

Obeagu, E.I., Scott, G.Y., Amekpor, F., Ofodile, A.C. and Chukwueze, C.M. (2023). A Systematic Review on the role of untreated inflammation of the genital tract in SARS COV 2 transmission. Madonna University Journal of Medicine and Health Sciences. 3 (1): 19-24.

Access this Article in Online	
	Website: www.ijarbs.com
Quick Response Code	Subject: Medical Sciences
DOI:10.22192/ijarbs.2023.10.03.020	

How to cite this article:
Emmanuel Ifeanyi Obeagu, Swalehe Hamisi and Umi Omar Bunu. (2023). An update on cytokine storm in covid-19 infection: Pivotal to the survival of the patients. Int. J. Adv. Res. Biol. Sci. 10(3): 171-180.
DOI: http://dx.doi.org/10.22192/ijarbs.2023.10.03.020