International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 03 Issue 10 October 2020
DOI: 10.47191/ijcsrr/V3-i10-03, Impact Factor: 6.595
IJCSRR @ 2020
www.ijcsrr.org

Immune Response to SARS-CoV-2 Infection

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Abstract: In December 2019 a new type of coronaviruses appeared in China and named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the disease associated with this virus is called Coronavirus Disease 2019 or COVID-19. Currently, COVID19 is the main global health threat. In this review, we focus in the current knowledge of immune response to SARS-CoV-2. Dysregulation of immune system, such as elevation levels of proinflammatory mediators and their roles in disease progression and pathogenesis as well as imbalance between innate and adaptive immune cells, are discussed in this review.
Key words: Innate immunity, adaptive immunity, coronavirus, COVID-19, SARS-CoV-2, Immune response.

Introduction

Coronaviruses are enveloped viruses with a single-stranded RNA. The genomes size is about 30–32 kb (1,2). The first human coronavirus was reported on 1966 by Tyrrell and Bynoe, named B814 (1,3). In the same period, Hamre and Procknow reported another strain of human corona virus called 229E (3,4). One year later, McIntosh et al reported multiple strains of human respiratory tract virus named as OC strains (e.g OC43) (5). In 1975, this new group of viruses has been given the name coronavirus, because of crown-like shape (6).

In 2002, a new form of human pathogenic corona virus was reported in China and named Severe Acute Respiratory Syndrome Corona (SARS-CoV). This virus was reported in twenty-nine countries around the world (7,8) and a total of 8098 individuals were infected with this type of virus with total fatalities of 774 (9). It was suggested that transmission of SARS-CoV is primarily from person to person via respiratory secretion but exact mode of transmission still unclear. The possible reservoirs for this corona virus were reported to be Himalayan palm civets and raccoon dogs (7-10).

Since 2003, six new human coronaviruses have been discovered including NL63 (11), NL (12), New Haven coronavirus (HCoV-NH) (13), HKU1 (14), Middle East Respiratory Syndrome (MERS) (15) and SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19) (16,17).

The SARS-CoV-2

The SARS-CoV-2 is closely related to SARS-CoV, both are belonging to beta-coronavirus genera (1). The virion of SARS-CoV-2 is about 50-200 nm in diameter, consists of four main proteins; the first three protein (spike (S), envelope (E), and membrane (M)) are located on the envelope of the virus and the fourth one is located on the nucleocapsid (N). The S protein facilitates the entry of the virus into host cell, after binding to a specific receptor on the host cells. This receptor has been identified as Angiotensin-Converting Enzyme 2 (ACE2), expressed by many cell types including cells of lungs, kidney, heart, arteries, intestines(1,2,18,19) and immune system (18,20).

Although the transmission mode is still not clear yet, but it was suggested that the virus can be transmitted through coughing, sneezing and close breathing from an infected individual or by hand after touching contaminated objects with the virus (21). SARS-CoV-2 infection is initiated by the interaction of the viral S proteins with ACE2 on host cells. After viral entry into the target cells, viruses undergo sequential events of RNA replications that eventually lead to dysfunction of infected cells. (1,2).

The most common symptoms of COVID-19 are pneumonia, fever, dry cough, tiredness and dyspnea (1,2). It has been shown that the mortality rate increases with increasing age or presence of co-morbidity such as diabetes mellitus (DM) (22). This can be attributed to the efficacy of the immune system, but this conclusion still premature yet.

Current available data indicates involvement of both innate and adaptive immune system components in the pathogenesis of COVID-19, including interferons (IFNs) response, high levels of circulating proinflammatory cytokines, lymphopenia, lymphocytes imbalance and extensive pulmonary infiltrates of mononuclear cells (1,2,22). This review focuses on immune response to SARS-COV-2 infection.

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Innate Immune response to SARS-CoV-2

To date, studies on the innate immune response to SARS-CoV-2 are still limited. However, findings from SARS-CoV may provide evidences for immune response to SARS-CoV-2 because of shared sequence homology between these two strains (1,2).

The innate immune components that may contribute to viral immune response in respiratory system includes soluble proteins such as IFNs, surfactant proteins that bind to viral particles and leukocytes (e.g alveolar macrophages, and natural killer (NK) cells) that engulf and kill invaders by using Pattern Recognition Receptors (PRRs), these receptors sense molecular patterns on pathogens, cause cell activation and cytokines and chemokines production, which induce an antiviral response. PRRs can be found on the cell surfaces or in the cytoplasm of variety of cells types including cells of immune systems such as macrophages and T cells. Example of cytoplasmic PRRs that can recognise viral molecular pattern including RIG-I (Retinoic acid-inducible gene I) and MDA5 (Melanoma Differentiation-Associated protein 5), collectively known as the RIG-I-like receptors (RLRs), along with endosomal Toll-like receptor 3 (TLR3) and TLR7. Activation of these receptors by RNA viral recognition induces type 1 IFNs response (23-25).

Type I IFNs response is mediated by a group of interferons including IFN-α along with IFN-β, IFN-ε, IFN-κ, IFN-ω, IFN-δ, IFN-ζ, and IFN-τ. These cytokines are rapidly produced after PRR engagement, subsequently, influence development of immune responses to infections and promoting generation of effectors and memory T and B cell (24-27). Type II IFNs immune response is mediated by IFN-□, predominantly produced by NK cells during viral infection, and has been shown to inhibit viral replication (26). In human, Type III IFN immune response is facilitated by IFNλ1(IL-29), IFNλ2 (IL-28A), IFNλ3 (IL-28B) and IFNλ4 (27). It has been shown that IFNλs have effective antiviral responses and can reduce the excessive production of proinflammatory cytokines such as Tumour Necrosis factor (TNF), interleukin (IL)-1β, IL-6, IL-12, and IFN-γ and chemokines such as IL-8, MCP-1 and IP-10. These cytokines are a common complication of respiratory infections caused by influenza A, SARS-CoV and MERS-CoV (24-29).

In case of RNA viruses, these pathways (in particular type I/III interferons) are initiated through the engagement of both cytoplasmic RLRs and cell membrane PRRs (e.g TLRs). Engagements of these receptors trigger downstream signaling cascades eventually activate secretion of proinflammatory cytokines such as TNF-□, and IL-1□, IL-1 Receptor Antagonist (IL-1RA) IL-6, IL-7, and IL-18 (23,25,27).

Evidences from SARS-CoV (30), MERS coronavirus (31) and recently SARS-CoV-2, IFN-I response effectively able to reduce CoV infection (32,33). Interestingly, invitro study showed that SARS-CoV-2 is more sensitive to IFN-I/III than SARS-CoV-1 (32).

Raised levels of cytokines and chemokines including: IL-1□, IL1RA, IL-2, IL-6, IL-8,IL-10, IL-17,TNF-□, IP-10, CXCL2, CXCL8, CXCL9, CXCL16, CXCL9, CXCL16, CCL8, CCL2, CCL3, G-CSF, GM-CSF, and MCP1, were observed in COVID-19 patients (34-39). These proinflammatory cytokines and chemokines may be the primary players on the pathogenesis, hyperinflammation and massive pulmonary infiltration of inflammatory cells (neutrophils, monocytes/macrophages) seen in COVID-19 patients and correlated with disease severity (34-38).

Recent studies showed that innate immune cells such as macrophages and dendritic cells play a central role in the inflammatory progression in COVID-19 patients (35-37). Type 1 macrophages (M1) respond to foreign substances via PRR and produce inflammatory molecules that can eliminate pathogens, whereas Typ2 macrophage (M2) triggers release of anti-inflammatory cytokines, which limit inflammation and promote tissue repair. Dendritic cells are known as a typical antigen presenting cells that involve in T cell activation. Hyperactivation of these cells can be damaging to the host (35-37). Moreover, the above cytokine profiles observed on COVID-19, show similarities to those observed in macrophage activation syndrome (36,37,38). Thus, it can be concluded that dysregulated activation of macrophages is the main cause of massive production of inflammatory cytokines and chemokines (which leads to cytokines storm) that was detected in COVID-19 patients (36,37,38). Therefore, inhibition of macrophages activation and blockades of these pro/ inflammatory cytokines such as IL-6 (36) and IL1□□□□□□ may provide an effective treatment for COVID-19.

Virgilio et al suggested that macrophage can be inhibited via P2X7 receptor (P2X7R) (40). Indeed, this suggestion is very valid, hence this receptor is expressed by mononuclear cells. Activation of this receptor triggers downstream-signaling cascades, resulting in profound production of proinflammatory cytokines, including IL-1□□□□□□. Moreover, we and others demonstrated that

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polymorphism at position 1068 and 1513 in the P2X7R gene might contribute to the pathogenesis of RA via accelerated production of proinflammatory cytokines (41,42). This finding may be applicable to COVID-19 patients, hence viral infection may cause a significant increase in ATP, a P2X7 ligand (43).

The complement proteins are considered as effective arm of innate immune system, activation of these proteins contributes to acute and chronic inflammation. Similarly, to cytokines and chemokines, hyperactivation of complement system may lead to anaphylactic shock and multiple organ failure (44,45). Several studies reported that complement system plays a key role in the pathogenesis of COVID-19 (45).

Moreover, postmortem analysis showed that elevated level of complement components mannose-binding lectin (MBL), C4, C3, and the terminal membrane attack complex C5b-9 in alveolar epithelial cells. Serum level serum C5a in COVID-19 patients have been found to be elevated (45,46). Histochemical analysis of kidney biopsies of COVID-19 patients revealed a strong C5b-9 complex deposition on kidney tubules demonstrating that complement system may contributes to the kidney failure in COVID-19 patients.

Nevertheless, other innate immunity inflammatory markers such as C- reactive protein, ferritin, D- dimers and procalcitonin are found to be elevated in COVID-19 patients (38,47). CRP and procalcitonin are associated with high risks of mortality and organ malfunctions (48).

Adaptive immune response to SARS-CoV-2

It is yet unclear whether humoral response or cell mediated immunity of the adaptive immunity confers the most protective immunity in COVID-19 patients. Several recent studies showed dysregulations of adaptive immune response in patients with COVID-19(35,38,49-52). Several studies showed that SARS-CoV-2 infection alters CD4+ and CD8+ T cells proportion, T regulatory cells and neutrophil-lymphocyte-ratio, particularly in severe cases of COVID-19 (38,49), Moreover, total lymphocytes, CD4+ T cells (T Helper cells and regulatory T cells), CD8+ T cells, NK cells, monocytes, eosinophils and basophils have been shown to be decreased in COVID-19 patients, and severe cases had a lower level than mild cases (36,38). Moreover, the expression of IFN-γ by CD4+ T cells, CD8+ T cells and NK cells tended to be lower in severe cases than in moderate cases with increased expression of CD94/NK group 2 member A (NKG2A) receptor. However, this abnormality is restored after recovery (53-56). Neutrophil lymphocyte-ratio (NLR) in COVID-19 patients has been found to be imbalanced and correlated with the severity of the disease (38,49). Moreover, it was suggested that NLR and changes in the count of lymphocyte subsets can be used as diagnostic markers for early screening of critical illness (38).

Disproportion of naïve versus memory T cells in favor of Naïve T cells was also reported. This scarcity of immunological memory development after natural active immunity can be implicated in the complexity of vaccine development for COVID-19 (38, 53, 54).

Changes in humoral immune response in COVID-19 patients were also reported. it has been shown that high level of plasma cells and decreased level of naïve B cells was observed in COVID-19. These changes also affected novel B cells receptors (BCRs) including's IGHV3-23 and IGHV3-7, and isotypes IGHV3-15, IGHV3-30, and IGKV3-11 (55,57).

Based on recent studies, antibodies to SARS-CoV-2 develop between 6–15 days after infection (57) and may remain over the course of seven weeks (58), which is much shorter period in comparison to SARS-COV-1 infection (52).

Concluding Remarks

- Current knowledge about immune response to SARS-COV-2 appears to be different from immune response in the other coronavirus infections.
- Components of innate and adaptive immune response seem to be key players on the pathogenesis of COVID-19.
- Proinflammatory cytokines, chemokines and complement pathways mediate hyperinflammation and severity of COVID-19.
- Blocking of these inflammatory processes could be a promising therapeutic approach for COVID-19.

References

1. Harapan H, Itoh N, Yufika A, Winardi W, Keam S, Te H, et al. Coronavirus disease 2019 (COVID-19): A literature review. J Infect Public Heal 2020; 13:667-673. doi: 10.1016/j.jiph.2020.03.019.

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2. Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbuto V, Veronese N, .et al. Coronavirus Diseases (COVID-19) Current Status and Future Perspectives: A Narrative Review. Int J Env Res Pub He 2020; 14;17 (8):2690. doi: 10.3390/ijerph17082690.
3. Tyrrell DA, Bynoe ML, (1966) Cultivation of viruses from a high proportion of patients with colds. Lancet 1:76–77. DOI: 10.1016/s0140-6736(66)92364-6.
4. Hamre D, Procknow JJ (1966): A new virus isolated from the human respiratory tract. Proc. Soc Exp Biol Med 121:190–193. doi: 10.3181/00379727-121-30734 P
5. McIntosh K, Dees JH, Becke WB, Kapikian AZ, Chanock RM. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. Proc Natl Acad Sci USA 1967; 57:933–940. doi:10.1073/pnas.57.4.933
6. Tyrrell DA, Almeida JD, Cunningham CH, Dowdle WR, Hofstad MS et al. Coronaviridae. Intervirol 1975; 5:76-82. doi: 10.1159/000149883.
7. Drosten C, Günther S, Preiser W, van der Werf S, Brodt HR, Becker S, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome see comment. N Engl J Med 2003; 348:1967–1976. doi: 10.1056/NEJMoa030747
8. Ksiazek TG, Erdman D, Goldsmith CS, Zaki R, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome see comment. N Engl J Med 2003; 348:1953–1966. . doi: 10.1056/NEJMoa03078.
9. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Available at: http://www.who.int/csr/sars/country/table2003_09_23/en/ (accessed 7 July 2020).
10. Hui DSC, Chan MCH, Wu1 AK, Ng PC. Severe acute respiratory syndrome (SARS): epidemiology and clinical features. Postgrad Med J 2004; 80:373-81. doi: 10.1136/pgmj.2004.020263.
11. van der Hoek L, Pyrc K, Jebbink MF, Vermeulen-Oost W, Berkhout RJM, Wolthers KC, et al. Identification of a new human coronavirus. Nat Med 2004; 10:368 –373. doi: 10.1038/nm1024
12. Fouchier RAM, Hartwig NG, Bestebroer TM, Niemeyer B, de Jong JC, Simon JH, et al. A previously undescribed coronavirus associated with respiratory disease in humans. P Natl Acad Sci USA 2004: 101:6212– 6216. doi:10.1073/pnas.0400762101
13. Esper F, Weibel C, Ferguson D, Landry ML, Kahn JS. Evidence of a novel human coronavirus that is associated with respiratory tract disease in infants and young children. J Infect Dis 2005; 191:492– 498. doi: 10.1038/nm1024.
14. Woo PCY, Lau SKP, Chu C-M, Chan KH, Tsoi HW, Huang Y, et al. Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. J Virol 2005; 79:884 – 895. doi: 10.1128/JVI.79.2.884-895.2005.
15. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 2012; 367:1814–1820. doi: 10.1056/NEJMoa1211721.
16. Wu F, Zhao S, Yu B, Chen YN, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature 2020; 579. :265-269. doi:10.1038/s41586-020-2008-3
17. World Health Organization https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it. (Accessed 7 July 2020).
18. Hamming I, Timen W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004; 203: 631–637. doi:10.1002/path.1570.
19. Donoghue M, Hsieh F, Baronas E, Godbout K, Gosselin M, Stagliano N, et al. A Novel Angiotensin-Converting Enzyme–Related Carboxypeptidase (ACE2) Converts Angiotensin. Circ Res 2000; 87: E1-9. doi: 10.1161/01.res.87.5.e1
20. Wan Y, J. Shang, R. Graham, R.S. Baric, F. Li. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. J Virol 2020; 94:e00127-20. doi: 10.1128/JVI.00127-20.
21. Rothan HA, Byraredd SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020; 109:102433. doi: 10.1016/j.jaut.2020.102433.
22. Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. J Med Virol 2020; 92:548-551. doi: 10.1002/jmv.25722.

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IJCSRR @ 2020
www.ijcsrr.org

23. Koyama S, Ishii KJ, Coban C, Akira S. Innate Immune Response to Viral Infection. Cytokine 2008; 43:336-41. doi: 10.1016/j.cyto.2008.07.009.
24. Goritzka M, Makris S, Kausar F, Durant LR, Pereira C, Kumagai Y, et al. Alveolar macrophage-derived type I interferons orchestrate innate immunity to RSV through recruitment of antiviral monocytes. J Exp Med 2015; 212:699-714. doi:10.1084/jem.20140825.
25. Brisse M, Ly H. Comparative Structure and Function Analysis of the RIG-I-Like Receptors: RIG-I and MDA5. Front Immunol 2019; 10:1586. doi:10.3389/fimmu.2019.01586.
26. Lee AJ, Ashkar AA. The Dual Nature of Type I and Type II Interferons. Front Immunol 2018; 9:2061. doi: 10.3389/fimmu.2018.02061.
27. Trinchieri G. Type I interferon: friend or foe? J Exp Med 2010; 207:2053-2063. doi: 10.1084/jem.20101664.
28. Galani IE., Triantafylli V, Eleminiadou EE, Koltsida O, Stavropoulos A, Manioudaki M, et al. Interferon-lambda mediates non-redundant front-line antiviral protection against influenza virus infection without compromising host fitness. Immunity 2017; 46:875-890.e6. doi: 10.1016/j.immuni.2017.04.025.
29. Zhang W, Zhao Y, Zhang F, Wang Q, Li T, Liu Z, et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the perspectives of clinical immunologists from China. J Clin Immunol 2020; 214: 108393. doi: 10.1016/j.clim.2020.108393.
30. Channappanavar R, Fehr AR, Vijay R, Mack M, Zhao J, Meyerholz DK et al. Dysregulated Type I Interferon and Inflammatory Monocyte-Macrophage Responses Cause Lethal Pneumonia in SARS-CoV-Infected Mice. Cell Host Microbe. 2016; 19:181-193. doi: 10.1016/j.chom.2016.01.007.
31. Channappanavar R., Fehr AR, Zheng J, Wohlford-Lenane C, Abrahante JE, M. Mack M, et al. IFN-I response timing relative to virus replication determines MERS coronavirus infection outcomes. J Clin Invest 2019; 129:3625-3639. doi: 10.1172/JCI126363.
32. Lokugamage KG, Hage A, Schindewolf C, Rajsbaum R, Menachery VD. SARS-CoV-2 is sensitive to type I interferon pretreatment. Version 3 bioRxiv 2020; Apr 9:2020.03.07.982264. doi: 10.1101/2020.03.07.982264. (preprint).
33. Mantlo E, Bukreyeva N, Maruyama J, Paessler S, Huang C. Antiviral activities of type I interferons to SARS-CoV-2 infection. Antivir Res 2020; 179:104811. doi: 10.1016/j.antiviral.2020.104811
34. Sarzi-Puttini P, Giorgi V, Sirotti S, Marotto D, Ardizzone S, Rizzardini G, et al. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? Clin Exp Rheumatol 2020; 38:337-342.
35. Blanco-Melo D, Nilsson-Payant BE, Liu WC, Uhl S, Hoagland D, Møller R, et al. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. Cell. 2020; 181:1036-1045.e9. doi: 10.1016/j.cell.2020.04.026.
36. Mehta P, McAuley DF, Michael B, Sanchez E, Tattersall RS. Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395:1033–1034. doi: 10.1016/S0140-6736(20)30628-0.
37. Abassi Z, Knaney Y, Karram T, Heyman TSN. The Lung Macrophage in SARS-CoV-2 Infection: A Friend or a Foe? Front Immunol 2020; 11:1312. doi: 10.3389/fimmu.2020.01312.
38. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Xie C, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis 2020; ciaa248. doi: 10.1093/cid/ciaa248. Online ahead of print.
39. Monteagudo LA, Boothby A, Gertner E. Continuous Intravenous Anakinra Infusion to Calm the Cytokine Storm in Macrophage Activation Syndrome. ACR Open Rheumatology 2020; 2:276-282. doi: 10.1002/acr2.11135.
40. Virgilio FD., Tang Y, Sarti AC, Rossato M. A Rationale for Targeting the P2X7 Receptor in Coronavirus Disease 19 (Covid-19). Br J Pharmacol 2020; 10.1111/bph.15138. doi: 10.1111/bph.15138 (Epub ahead of print).
41. Al-Shukaili A, Al-Kaabi J, Hassan B. A comparative study of interleukin-1beta production and p2x7 expression after ATP stimulation by peripheral blood mononuclear cells isolated from rheumatoid arthritis patients and normal healthy controls. Inflammation 2008; 31:84-90. doi: 10.1007/s10753-007-9052-0.
42. Al-Shukaili A, Al-Kaabi J, Hassan B, Al-Araimi T, Al-Tobi M, Al-Kindi M, et al.P2X7 receptor gene polymorphism analysis in rheumatoid arthritis. Int J Immunogenet 2011; 38:389-96. doi: 10.1111/j.1744-313X.2011.01019.x.
43. Zhang C, He H, Wang L, Zhang N, Huang H, Xiong Q, et al. Virus-Triggered ATP Release Limits Viral Replication through Facilitating IFN-β Production in a P2X7-Dependent Manner. J Immunol 2017; 199:1372-1381.

doi: 10.4049/jimmunol.1700187.
44. Noris M, Benigni A, Remuzzi G. The case of Complement activation in COVID-19 multiorgan impact. Kidney Int 2020; 2538: 30556-30551. doi: 10.1016/j.kint.2020.05.013. Online ahead of print.
45. Gao T, Hu M, Zhang X, Li H, Zhu L, Liu H, et al. Highly pathogenic coronavirus N protein aggravates lung injury by MASP-2-mediated complement overactivation. medRxiv 2020; Available at: https://www.medrxiv.org/content/10.1101/2020.03.29.20041962v2. doi: 10.1101/2020.03.29.20041962.
46. Diao B, Wang C, Wang R, Feng Z, Tan Y, Wang H, et al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. medRxiv 2020; Available at: https://www.medrxiv.org/content/10.1101/2020. 03.04.20031120v4. doi: https://doi.org/10.1101/2020.03.04.20031120.
47. Thirumalaisamy PV, Meyer CG. Mild Versus Severe COVID-19: Laboratory Markers. Int J Infect Dis 2020; 95:304-307. doi: 10.1016/j.ijid.2020.04.061.
48. Li D, Chen Y, Liu H, Jia Y, Li F, Wang W, et al. Immune dysfunction leads to mortality and organ injury in patients with COVID-19 in China: insights from ERS-COVID-19 study. Signal Transduct Target Ther 2020; 5, 62. doi: 10.1038/s41392-020-0163-5.
49. Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HHX, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect 2020; 81: e6-e12. doi:10.1016/j.jinf.2020.04.002
50. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease. J Clin Invest 2020; 130:2620-2629. doi: 10.1172/JCI137244.
51. Liu Z, Long W, Tu M, Chen S, Huang Y, Wang S, et al. Lymphocyte subset (CD4+, CD8+) counts reflect the severity of infection and predict the clinical outcomes in patients with COVID-19. J Infect 2020 S0163-4453(20)30182-1. doi: 10.1016/j.jinf.2020.03.054. Online ahead of print.
52. Wang F, Nie J, Wang HQ, Zhao Q, Xiong Y, Deng L et al. Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia. J. Infect Dis 2020; 221:1762-1769.
53. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther 2020; 5(1):33 doi:10.1038/s41392-020-0148-4
54. Wen W, Su W, Tang H, Le W, Zhang X, Zheng Y, et al. Immune cell profiling of COVID-19 patients in the recovery stage by single-cell sequencing. Cell Dis 2020; 6:31. doi:10.1038/s41421-020-0168-9
55. Wan WY, Lim SH, Seng EH. Cross-reaction of sera from COVID-19 patients with SARS-CoV assays. medRxiv 2020; 2020.03.17.20034454. doi: https://doi.org/10.1101/2020.03.17.20034454.
56. Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Cell Mol Immunol 2020; 17:533-535. doi: 10.1038/s41423-020-0402-2.
57. Xiao AT, Gao C, Zhang S. Profile of specific antibodies to SARS-CoV-2: The first report. J Infect 2020; 81:147-178. doi: 10.1016/j.jinf.2020.03.012.
58. Wu LP, Wang NC, Chang YH, Tian XY, Na DY, Zhang LY, et al. Duration of antibody responses after severe acute respiratory syndrome. Emerg infect Dis 2007; 13:1562-1564. doi: 10.3201/eid1310.070576.

Cite this Article: Dr. Ahmed Al-Shukaili (2020). Immune Response to SARS-CoV-2 Infection. International Journal of Current Science Research and Review, 3(10), 113-118