REVIEW ARTICLE

Association of COVID-19 with Pancreatic and Nutritional Disorder: A Comprehensive Summary

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Introduction

With the insurgence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the city of Wuhan, China, coronavirus disease 2019 (COVID-19) has been declared as a global pandemic by the WHO. It mainly involves respiratory system but there are some evidences implying its involvement with liver, kidney and heart also. There is a paucity of data regarding the association of COVID-19 with pancreatic injury or nutritional disorders. This is a comprehensive review of systemic literature search of the data from Pubmed and Cochrane databases published after December 2019, with key words "COVID-19", "SARS-Cov-2", "pancreas", "nutrition" , "malnutrition", "breast feeding" etc.

Pancreatic Disorders

Spike protein, which is one of the main structural proteins of SARS-CoV-2, binds with angiotensin-converting enzyme 2 (ACE2) protein of the host cell membrane to fuse into the cell for nucleic acid replication. ACE2 is not only expressed in alveolar epithelial cells, but also in the heart, gastrointestinal tract, kidney, testis and other organs, which means that SARS-CoV-2 is likely to enter other tissues and organs through ACE2 binding, causing multiple organ damage.[1] In an unrefereed preprint retrospective and observational study , it was observed that some patients showed signs of pancreatic injury, such as high levels of amylase and lipase in serum and urine, implying that pancreas too is a vulnerable organ. They showed that ACE2 is expressed in both the exocrine glands and islets, and the expression is more than that seen in lungs.[2]

In a study of 52 COVID diagnosed patients, pancreatic injury was seen in 17%. It was also observed that patients with pancreatic injury had higher incidence of other morbidities as anorexia, diarrhea etc. Pancreatic involvement was postulated to be a result of direct cytopathic effect of local SARS-CoV-2 replication or due to an indirect systemic immune response to the viral infection or respiratory failure.[3]

Nutritional Disorder

Nutrition in COVID -19 is as important as in any other morbid disease and might influence the outcome. Among other risk factors as co-morbidities and older age, COVID-19 has poor outcome in hypoalbuminemic patients. It has been postulated that patients with older age and comorbid conditions are mostly associated with poor nutritional status and sarcopenia , which might be one of the causes for poor outcome.[4] Lymphopenia, which is also a marker of malnutrition, and low prealbumin are considered as poor prognostic indicators for COVID-19 .[5,6]

China Medical Treatment Expert Group for Covid-19 from Guangzhou Institute of Respiratory Health published data regarding 1099 patients with laboratory-confirmed Covid-19 from 552 hospitals in China. The median age of the patients was 47 years, 41.9% being females. This observational study does not mention any nutrition related problem or any special nutritional requirement in the admitted patients, though no nutritional assessment was done in these patients at the time of admission. Fever developed in 88.7% patients during hospitalization but nausea or vomiting (5.0%) and diarrhea (3.8%) were uncommon.[7] Patients with active-stage IBD with malnutrition are included in the potential risk factor group , however, no such patients have been reported to be infected with SARSCoV-2 so far.[8] In a series of 34 children from China with median age 8 years and 11months, the disease was mild and no nutritional ailment has been reported. [9] In the largest pediatric series of 2,143 children with median age 6.7 years at Wuhan Children's Hospital, no nutritional co-morbidities or consequences have been described. [10]

Nutritional Management of COVID-19 Patients

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends screening and maintenance of nutrition for all patients diagnosed as COVID-19 or admitted in ICU and suggests that every patient staying for more than 48 hours in ICU should be considered at risk for malnutrition**.** Energy and protein can be administered orally, enterally or parentally depending upon patient's condition. Hypocaloric nutrition should be administered in the early phase of acute illness, which should not exceed 70% of the energy expenditure, increasing gradually

up to 80-100% after 3 days. To preserve the skeletal mass and enhance muscle anabolism during ICU stay, daily protein 1.3gm/kg/day should be administered. Regular physical activity and mobilisation is important for the beneficial effect of the administered nutrition in patients. Diet rich in eicosapentaenoic acid, gamma-linolenic acid, and antioxidant agents in patients with ARDS or acute lung injury improves oxygenation. [11]

WHO advises to maintain hydration by drinking enough water, and have a well-balanced diet to boast up the immune systems and lower the risk of chronic illnesses and infectious diseases. It is important to have fresh and unprocessed foods every day to get the vitamins, minerals, dietary fibre, protein and antioxidants . Excess sugar, fat and salt should be avoided to lower the risk of obesity, heart disease, diabetes etc. [12]

Nutritional support and application of prebiotics or probiotics are suggested to regulate the balance of intestinal microbiota and reduce the risk of secondary infection due to bacterial translocation.[13]

Breastfeeding in COVID-19 Pandemic

So far, presence of SARS- CoV-2 in the breast milk has not been demonstrated and there is no evidence that it could be transmitted through breast milk. Considering the benefits of the breastfeeding, baby can be directly fed even if the mother is previously identified as COVID-19 positive or is under investigation for COVID-19 but is asymptomatic or pauci-symptomatic. Mother should wear a proper mask and follow strict measures of infection control. If the mother is very sick, fresh expressed breast milk can be fed. [14,15,16]

Role Micronutrients

Micronutrients play an important role in immunity boost up in patients with COVID-19 specially those who are malnourished.

Vitamin D: Apart from enhancing bone growth, vitamin D stimulates maturation of many cells including immune cells. Based on some observational studies and clinical trials that reported the utility of vitamin D supplementation to reduce the risk of influenza, and that vitamin D deficiency has been found to contribute to acute respiratory distress syndrome, it is recommended that people at risk of COVID-19 should consider taking vitamin D_3 for a few weeks to rapidly raise 25(OH)D concentration. [17]

Vitamin A: Vitamin A is also called "anti-infective" vitamin. Its supplementation has been shown to prevent morbidity and mortality in many viral illnesses as diarrhea, measles etc, and other infections as malaria and lung infections. The mechanism is supposed to be the up regulation of the innate immune response in uninfected bystander cells, making them refractory to infection during subsequent episodes of viral invasion. In an experiment with chickens infected with infectious bronchitis virus, a type of coronavirus, the chickens that were fed adequate vitamin A were less affected than those who were deficient. [11]

B Vitamins: It has been observed that vitamin B2 and UV light effectively reduced the titer of MERS-CoV in human plasma products, vitamin B3 significantly inhibited neutrophil infiltration into the lungs with a strong anti-inflammatory effect and vitamin B6 is needed in protein metabolism and many reactions in body tissues and also plays important roles in body immune functions. So, it can be inferred that adequate supplementation of B vitamins might augment the host immune response in COVID-19 patients as well. [18]

Vitamin C: Vitamin C acts as an antioxidant and has been shown to uplift the immune functions and protect against infection caused by SARS coronavirus. In one study, it also increased the resistance of chick embryo to avian coronavirus. Functioning as a weak anti-histaminic agent it can provide relief in flu-like symptoms such as sneezing, running or stuffy nose. It has also been shown in human trials that vitamin C lowers the susceptibility to lower respiratory tract infections. So, vitamin C could be one of the effective choices for the prevention and supportive treatment of COVID-19. [18, 19]

Vitamin E: Vitamin E reduces the oxidative stress and has been shown to prevent bovine coronavirus infection in calves. It can be a useful supplement in COVID-19 as well. [19]

Zinc: Zinc is important for the development of our immune system. Zinc deficiency can lead to increase susceptibility to infectious diseases. It is beneficial in lower respiratory tract infection and diarrhea by the stimulation of epithelial growth. It has also been shown that surge in intracellular zinc concentration with zinc-ionophores like pyrithione can efficiently impair the replication of a variety of RNA viruses like SARS-coronavirus. Therefore, zinc supplementation may have role in COVID-19 management. [19]

Iron: It has been shown on molecular level that the viral structural proteins attack the heme on the 1-beta

chain of hemoglobin to dissociate the iron to form the porphyrin leading to drop in hemoglobin resulting in poor oxygen carrying capacity of the red blood cells. Also, the antigen-antibody reaction after the viral invasion leads to immune hemolysis. Iron deficiency is considered one of the risk factors for respiratory tract infections .But the role of iron supplementation is not clear in COVID-19. [19]

Conclusion

COVID-19 is known so far to primarily involve the respiratory system, but there are evidences to show the involvement of other organs as well like pancreas. Though there is little evidence that COVID-19 impairs the nutritional status of the patients but malnutrition has been postulated as one of the poor prognostic markers and prolonged illness or ICU stay may lead to nutritional deficiencies and loss of skeletal mass leading to poor outcome and convalescence. Many micronutrients have been shown to have immunity booster effects and advantageous in coronavirus infection. Therefore it is very prudent to focus on the nutritional status of the COVID-19 affected patients.

Bibliography

1. Hamming I, Timens W, Bulthuis ML, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004; 203:631-7.
2. Furong Liu, Xin Long, Wenbin Zou et al. Highly ACE2 Expression in Pancreas May Cause Pancreas Damage After SARS-CoV-2 Infection. medRxiv 2020.02.28.20029181; doi: https:// doi.org/10.1101/ 2020.02.28.20029181.
3. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q, Pancreatic injury patterns in patients with COVID-19 pneumonia. Gastroenterology 2020. doi: https://doi.org/10.1053/ j.gastro.2020.03.055.
4. Graf CE, Pichard C, Herrmann FR, Sieber CC, Zekry D, Genton L. Prevalence of low muscle mass according to body mass index in older adults. Nutrition 2017; 34:124–9.
5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohortstudy.Lancet 2020; 395:1054–62.
6. WuC, ChenX, etal. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus Disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020. https://doi.org/ 10.1001/jamainternmed.2020.0994.
7. W. Guan, Z. Ni, Yu Hu, W. Liang et al. Clinical Characteristics of Coronavirus Disease 2019 in China. The New England journal of medicine. February 28, 2020, at NEJM.org. DOI: 10.1056/NEJMoa2002032.
8. Ren Mao, Jie Liang, Jun Shen et al. Implications of COVID-19 for patients with pre-existing digestive diseases. Lancet Gastroenterol Hepatol 2020. Published Online March 11, 2020. https://doi.org/10.1016/ S2468-1253(20)30076-5.
9. Chen F, Liu ZS, Zhang FR, et al. First case of severe childhood novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi. 2020;58: E005.
10. Wei M, Yuan J, Liu Y, et al. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. Jama 2020;14:14. doi:https://dx.doi.org/10.1001/jama.2020.2131
11. Barazzoni R et al., ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection, Clinical Nutrition. https://doi.org/10.1016/ j.clnu.2020.03.022.
12. http://www.emro.who.int/nutrition/ nutrition-infocus/nutrition-advice-for-adults-during-the-covid-19-outbreak.html
13. COVID-19): the Zhejiang experience. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020 Feb 21;49.
14. Chen H.,Guo ,Wang C, et al. Clinical

characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. Lancet, 359(10226), 809–815. doi:10.1016/S0140-6736(20)30360-3.

15. Rasmussen,Smulian, et al . Coronavirus disease 2019 (COVID-19) and pregnancy: What obstetricians need to know.American Journal of Obstetrics and Gynecology. doi:10.1016/j. ajog.2020.02.01.
16. Davanzo R, Moro G et al. Breastfeeding and Coronavirus Disease-2019. Ad interim indications of the Italian Society of Neonatology endorsed by the Union of European Neonatal & Perinatal Societies. Matern Child Nutr. 2020 Apr 3:e13010. doi: 10.1111/mcn.13010
17. Grant WB, Lahore H, et al. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. Nutrients 2020 Apr 2;12(4). pii: E988. doi: 10.3390/nu12040988.
18. Zhang L, Liu Y. Potential Interventions for Novel Coronavirus in China: A systematic Review.J Med Virol 2020;92:479-90.
19. Hemila, H. Vitamin C and SARS coronavirus. J. Antimicrob. Chemother. 52, 1049-1050, doi:10.1093/jac/dkh002 (2003).
20. COVID-19): the Zhejiang experience. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020 Feb 21;49.