ISSN: 2583-5386
DOI: doi.org/10.51219/Zahra-Meshkat/8

URF PUBLISHERS
connect with research world

Journal of Integrated Health

https://urfpublishers.com/journal/integrated-health

Vol: 2 & Iss: 3

Mini-Review

Microbiota and COVID -19: Microbial Dysbiosis

Mostafa Fazeli[1], Nader Yazdinezhad[2], Zahra Meshkat*[3]

[1] Department of Medical Genetics and Molecular Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Department of Virology, Lorestan University of Medical Sciences, Khorramabad, Iran

[3]Antimicrobial Resistance Research Center, Mashhad University of Medical Sciences, Iran

Citation: Fazeli M, Yazainezhad N, Meshkat Z. Microbiota and COVID -19: Microbial Dysbiosis. *J. Integrated Health*, 2(3), 52-54. DOI: doi.org/10.51219/Zahra-Meshkat/8

Received: 08 August, 2023; **Accepted:** 31 August, 2023; **Published:** 06 September, 2023

***Corresponding author:** Zahra Meshkat, Antimicrobial Resistance Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. P.O Box: 9196773117, Tel: +98-5138012453, Fax: +98-5138002960, Mashhad, Iran. E-mail: meshkatz.mums.ac.ir@gmail.com

A B S T R A C T

SARS-CoV-2 causes an acute respiratory syndrome named COVID-19. This virus spread across the globe rapidly and started a pandemic. Many researchers are pursuing finding the mechanisms involved in the disease course and methods of controlling them. In addition to respiratory symptoms, COVID-19 demonstrates digestive symptoms; These findings suggest that microbiota might play a role in the development of COVID-19. Studies showed that lung and gut microbiota composition could change by SARS-CoV-2, and microbial dysbiosis affects disease development and severity. Based on these findings, manipulation of the microbiota utilizing diet, antibiotics, prebiotics, or probiotics can be beneficial in COVID-19 management and improving vaccine efficiency.

Keywords: COVID 19, microbiota, gut, microbiome, dysbiosis.

Abbreviation: COVID-19: Coronavirus disease 2019, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, GI: Gastrointestinal, SCFAs: short-chain fatty acids, HCs: healthy controls, CRP: C-reactive protein, spp: species.

Introduction

COVID-19 emerged in the final days of 2019 and became a global health issue soon after that. COVID-19 is an acute respiratory disease that is caused by a novel Coronavirus known as SARS-CoV2. In addition to respiratory symptoms, digestive symptoms are also prevalent in patients with COVID-19; a meta-analysis reported that 20 percent of COVID-19 patients show digestive symptoms[1]. Moreover, viral RNA has been detected in fecal specimens [2, 3]. An increasing body of evidence suggests microbiota alteration during disease progression in the COVID-19, especially gut microbiota[2-7]. Understanding the role of microbiota in SARS-CoV2 infection mechanisms and its pathogenesis may be beneficial in improving disease management.

Microbiota

Microbiota is described as a microbial community that is consisted of archaea, bacteria, viruses, fungi, and protozoa that colonize the surfaces of a host's body. The genome of these microorganisms is known as the microbiome. They can influence the host's health and cause many diseases, such as metabolic diseases, neurodegenerative disorders, non-communicable or infectious diseases. The gut microbiome plays a vital role in overall health; however, our knowledge of the pulmonary microbiome is still low[8].

Lung and gut axis

The gut microbiome plays a vital role in the function and evolution of the host's immune response in the digestive system and other organs. this role is fulfilled by producing a

certain number of metabolites such as SCFAs. Recent findings point out a connection between 2 microbial populations in the gut and lung known as the gut-lung axis. Besides, Xu et al. reported that the upper respiratory system bacterial microbiome correlates with a gut microbial population during the COVID-19[9]. Gut microbiome conversion can affect pulmonary immune responses and lung homeostasis that mediates susceptibility to respiratory diseases[10]. In patients struggling with COVID-19, gut microbiome composition changes significantly[4-6]. A reduction in microbial diversity and also shifts in microbial composition have been observed in patients with dysbiosis. Additionally, microbial composition differs between patients based on their illness severity[11].

Microbiota and COVID 19

Viral composition

Checking viromes demonstrates a significant difference between COVID-19 patients and HCs. Members of *Herelleviridae* and *Virgaviridae*, bacteriophages, and some unclassified viruses have been recognized in the gut virome of COVID-19 patients. An abundance of some phages from *Inviridae* and *Microviridae* families and a member of the *Virgaviridae* family and unclassified viruses is significantly higher in COVID-19 patients than HCs[11].

Bacterial species alteration

Bacterial genera such as *Acinetobacter*, *Chryseobacterium*, *Burkholderia*, *Brevundimonas*, *Sphingobium*, and *Enterobacteriaceae* are most abundant in the pulmonary microbiome of COVID-19 patients[12]. Contrary to pulmonary microbiome, many studies have evaluated gut microbiome in COVID-19 patient, understanding that some bacterial genera and species including *Bifidobacterium* spp., *Lactobacillus* spp., *Clostridium* spp. such as *C. butyricum*, *C. leptum*, *Eubacterium* spp. such as *E. rectale*, *E. hallii* and *E. eligens* , *Alistipes* spp. such as *A. shahii* and, *A. indistinctus, Roseburia* spp. such as *R. intestinalis, Parasutterella excrementihominis, Coprobacter fastidiosus, Odoribacter splanchnicus, Ruminococcus bromii, Faecalibacterium* spp. such as *F. prausnitzii, Coprococcus* spp., and *Parabacteroides*, and *Sutterella* and also Burkholderiales bacteria , Bacterioidales bacteria such as, *Bacterioides salyersiae*, and *B. massiliensis* face a decline in population during the disease course, while *Corynebacterium, Ruthenibacterium*, *Streptococcus, Rothia, Veillonella, Actinomyces, Ruminococcus gnavus, Eggerthella* spp. such as *E. lenta, Coprobacillus, Lachnospiraceae* bacterium 2_1_58 FAA, *Lachnospiraceae* bacterium 1_4_56FAA, *Clostridium* spp such as *C. ramosum, Lactobacillus*, and *Bifidobacterium, Enterococcus* and *Enterobacteriaceae* such as *Escherichia* go through an amplification in their population[2, 4, 6, 11, 13].

Some bacterial genera such as *Bifidobacterium* spp., *Lactobacillus* spp., and *Clostridium* spp. have demonstrated different outcomes in different studies, which shows the need for more research to understand the dynamics of their population during the disease course [2, 4]. Some beneficial bacteria, especially those with immunomodulatory characteristics like *F. prausnitzii, E. rectale*, and bifidobacteria, remain low even after 30 days from recovery.

Microbial type correlates with disease severity. In stool samples with high viral load, *Collinsella aerofaciens, Collinsella tanakaei, Streptococcus infantis,* and *Morganella morganii* were more likely to be detected. On the contrary, *Parabacteroides merdae, Bacteroides stercoris, Alistipes onderdonkii*, and *Lachnospiraceae* bacterium were found more in people with low viral load or no viral load at all[3]. Zuo et al. observed an inverted connection between viral load in stool samples and some species of *Bacteroides* spp. such as *B. dorei, B. thetaiotaomicron, B. massiliensis,* and *B. ovatus*[7]. Disease severity is correlated to the abundance of *Coprobacillus Blautia*, *Clostridium ramosum* and *C. hathewayi, Ruminococcus*, however, unlike these bacteria, *F. prausnitzii, Bacteroides*, and Clostridiales have an inverted correlation with disease severity [11, 14]. In summary, under COVID-19 disease circumstances, bacterial diversity has declined significantly, as beneficial butyrate-producer bacteria have decreased in numbers while opportunistic pathogens have amplified.

Mycobiota

The diversity of stool mycobiome in COVID-19 patients is higher than HCs[15]. Additionally, in these patients, a decreased population in *Aspergillus* spp. and *Penicillium* spp., and an increased population in opportunistic pathogens including *Candida albicans, C. auris, C. glabrata*, and *Aspergillus flavus* were seen[15, 16]. After the recovery from respiratory symptoms and clearing virus, *A. flavus* and *A. niger* can still be detected in stool samples[15]. A correlation between Mucoromycota and *Fusicatenibacter* has been observed, in addition to a correlation between *A. niger* and diarrhea while *P. citrinum* shows an inverted correlation with CRP[16]. In the deceased cases of COVID-19, the most common fungal genera in pulmonary mycobiota have been *Cutaneotrichosporon, Issatchenkia, Wallemia, Cladosporium, Alternaria, Dipodascus, Mortierella, Aspergillus, Naganishia, Diutina*, and *Candida*.

Clinical Significance And Therapeutic Approaches

Correlation between gut microbial dysbiosis in COVID-19 patients and disease severity and hematological parameters has been observed[5]. The mentioned dysbiosis causes cytokine storm and increased blood markers like CRP and hepatic enzymes[6]. Cytokine storm might be connected to gut microbiota conversion caused by SARS-CoV2 viral infection, as levels of stool IL-18 have demonstrated correlation with relative abundancy of species of *Peptostreptococcus, Fusobacterium,* and *Citrobacter*[2]. Death by COVID-19 and severe respiratory symptoms can be predicted by gut and oral microbiome composition with 92 and 84 percent accuracy, respectively. This number reaches 96 percent for gut microbiota after being combined with symptoms and comorbidities[17].

Tang et al. believe that *Enterococcus* and *Enterobacteriaceae* can be used as biomarkers for COVID-19, and the *Enterococcus* to *Enterobacteriaceae* ratio can be utilized to predict death in patients with the acute disease[5]. Furthermore, Ward et al. found out that *Enterococcus faecalis* enrichment in patients can predict the disease severity[17]. Dysbiosis and some microbial species might be beneficial for diagnosis and even managing the disease better.

In animal models, recombinant *Lactobacillus plantarum* affects coronavirus infection in the gut. Some reports indicate beneficial uses of *L. rhamnosus* GG in maintaining healthy conditions in the gut and lung. Vaccine response enhancement against influenza virus respiratory infections has been observed while utilizing probiotic bacteria such as *Bifidobacterium*, *L. paracasei*, and *L. rhamnosus*[8]. Prebiotics and probiotics might be helpful in the management and treatment of COVID-19. Nevertheless, more research is needed in this matter.

Conclusion

During the COVID-19 disease, the microbiome that occupies the upper respiratory tract, lung and gut goes through many changes. This dysbiosis correlates with cytokine levels like IL-18 and some inflammatory markers in patients. These findings suggest the microbial dysbiosis' role in inflammation and immunologic procedures in COVID-19. There is evidence suggesting that imbalance in the microbial composition is related to disease severity.

Since microbiome changes by diet, probiotics, and prebiotics, and even consuming antibiotics, more studies are needed to assess its effect on COVID-19 outcomes and microbiota manipulation approaches that might effectively control the COVID-19 disease.

Conflict of Interest

There is no conflict of interest

References

1. Cheung KS, Hung IFN, Chan PPY, et al., *Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis.* Gastroenterology, 2020. **159**(1): p. 81-95.
2. Tao W, Zhang G, Wang X, et al., *Analysis of the intestinal microbiota in COVID-19 patients and its correlation with the inflammatory factor IL-18 and SARS-CoV-2-specific IgA.* medRxiv, 2020: p. 2020.08.12.20173781.
3. Zuo T, Liu Q, Zhang F, et al., *Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19.* Gut, 2021. **70**(2): p. 276.
4. Gu S, Chen Y, Wu Z, et al., *Alterations of the Gut Microbiota in Patients With Coronavirus Disease 2019 or H1N1 Influenza.* Clin Infect Dis, 2020. **71**(10): p. 2669-2678.
5. Tang L, Gu S, Gong Y, et al., *Clinical Significance of the Correlation between Changes in the Major Intestinal Bacteria Species and COVID-19 Severity.* Engineering, 2020. **6**(10): p. 1178-1184.
6. Yeoh YK, Zuo T, Lui GCY, et al., *Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19.* Gut, 2021. **70**(4): p. 698.
7. Zuo T, Zhang F, Lui GCY, et al., *Alterations in Gut Microbiota of Patients With COVID-19 During Time of Hospitalization.* Gastroenterology, 2020. **159**(3): p. 944-955.e8.
8. He LH, Ren LF, Li JF, Wu YN, Li X, Zhang L, et al., Intestinal Flora as a Potential Strategy to Fight SARS-CoV-2 Infection. Front Microbiol, 2020. 11: p. 1388-1388.
9. Xu R, Lu R, Zhang T, et al., *Temporal association between human upper respiratory and gut bacterial microbiomes during the course of COVID-19 in adults.* Commun Biol, 2021. **4**(1): p. 240.
10. Oliveira GLVD, Oliveira CNS, Pinzan CF, Salis LVVD, Cardoso CRDB, et al., *Microbiota Modulation of the Gut-Lung Axis in COVID-19.* Front Immunol, 2021. **12**(214).
11. Cao J, Wang C, Zhang Y, et al., *Integrated gut virome and bacteriome dynamics in COVID-19 patients.* Gut Microbes, 2021. **13**(1): p. 1-21.
12. Fan J, Li X, Gao Y, et al., *The lung tissue microbiota features of 20 deceased patients with COVID-19.* J Infect, 2020. **81**(3): p. e64-e67.
13. Yu L, Tong Y, Shen G, et al., *Immunodepletion with Hypoxemia: A Potential High Risk Subtype of Coronavirus Disease 2019.* medRxiv, 2020: p. 2020.03.03.20030650.
14. Gou W, Fu Y, Yue L, et al., *Gut microbiota may underlie the predisposition of healthy individuals to COVID-19.* medRxiv, 2020: p. 2020.04.22.20076091.
15. Lv L, Gu S, Jiang H, et al., *Gut mycobiota alterations in patients with COVID-19 and H1N1 infections and their associations with clinical features.* Commun Biol, 2021. **4**(1): p. 480.
16. Zuo T, Zhan H, Zhang F, et al., *Alterations in Fecal Fungal Microbiome of Patients With COVID-19 During Time of Hospitalization until Discharge.* Gastroenterology, 2020. **159**(4): p. 1302-1310.e5.
17. Ward DV, Bhattarai S, Correa MR, et al., *The intestinal and oral microbiomes are robust predictors of COVID-19 severity the main predictor of COVID-19-related fatality.* medRxiv, 2021: p. 2021.01.05.20249061.