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Understanding the Correlation of Diet, Immunity, and Probiotics: A Credible Implication in SARS-CoV2 Infections

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The COVID-19 had been emerged as a pandemic and resulted in more than 273 million reported cases and 5.3 million deaths worldwide. Concerns have been raised regarding this virus due to its unprecedented ability to move from human to human and cause infections, acute morbidity, and fatal outcome. Gut and lung microbiome profile substantially depends on dietary habits and plays a major role in modulating immunity thereby providing resistance to viral infections. The Gut-lung axis shows a correlation in microbial profile and the gastrointestinal microbiota can modulate lung microbiota majorly through the impact of microbial metabolites. Firmicutes and Actinobacteria specifically Bifidobacterium and Lactobacillus are responsible to modulate immunity and are widely used as probiotic species. In this review, we have concluded that different dietary habits affect microbial diversity and it can be a determining factor to fight SARS-CoV2 infections.

Keywords: Gut Microbiota and Diet; Immunomodulation; Lung Microbiota; Probiotics; SARS-CoV2.

The COVID-19 pandemic caused multiple deaths and a major burden on the healthcare system of the countries. According to the epidemiological report of WHO on 19th of December, 2021, over 273 million reported cases and 5.3 million deaths have been reported globally across 213 countries, areas, and territories [1]. Countries strictly followed containment steps and lockdown measures to cope with the spread of this infection. These steps, while important for preventing the spread of COVID-19 and reducing the number of deaths in the absence of successful therapies and vaccines, have resulted in substantial short-term economic losses. Containment measures have had, on average, a very large impact on economic activity equivalent to a loss of about 15 percent in industrial production over 30 days following their implementation [2]. Countries are trying several approaches based on a case-to-case basis and health care facilities. In general, the common drugs used in the pandemic by different countries are lopinavir, ritonavir, chloroquine, and remdesivir. According to the WHO's Draft landscape and tracker of COVID-19 candidate vaccines, 186 vaccine candidates are

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currently in the pre-clinical phase and 87 vaccines in the clinical phase. Some of the vaccines like Comirnaty by Pfizer, Moderna COVID 19 Vaccine by Moderna, Covishield by Astrazeneca, Sputnik V by Gamaleya Research Institute, CoronaVac by Sinovac, Covaxin by Bharat Biotech and COVID-19 Vaccine Janssen by Johnson & Johnson are currently in use in different countries[3]. In these vaccines, the Astrazeneca's vaccine Covishield has been reported several cases of unusual thrombotic events and thrombocytopenia after administration to some of the candidates [4]. These kinds of studies are limited with data and patient's studies and it will be too hurry to conclude the side effects and efficacy of these vaccines. Also, the strains of the virus are mutating rapidly resulting in different variants and it is going to be more challenging for any of the vaccines. The current variants included in the variant of interest by the United States are B.1.526, B.1.525, and P.2; while those included in the variant of concern by the United States are: B.1.1.7, P.1, B.1.351, B.1.427, and B.1.429. The discovery of double and triple mutant variants in India has resulted in a substantial increase in the number of cases [5]. Recently, a new SARS-CoV-2 variant of concern, omicron has been reported, which is showing the highest rate of transmissibility amongst other variants [6]. Vaccines and other kinds of medications are sought to fight the infections that exist in the community but it's not a precautionary measure. We need an alternative approach such as natural immunity boosters that may help us to fight and reduce the severity of this kind of infection.

The existing immunity is the first and most effective defensive barrier, responsible to prevent and fight different infectious diseases. Various studies have found that similar to the gut, human lungs also have a protective shield of microbes, specifically in the upper and lower respiratory zone that protects us from viral, bacterial, and fungal infections [7]. Any disturbance in the microbial environment makes us prone to infections [8]. Like other respiratory viruses, SARS-CoV2 also must face the microbial environment of the lining of the respiratory tract. It is therefore pertinent that a good microbiota profile may also play a role in the vulnerability of SARS-CoV2 infection. The microbial diversity of lung microbiota depends on lifestyle, exposed environment while some studies observed that gut microbiota environment also influences the diversity of the lung microbiota in many ways [9,10]. More precisely, the diversity of gut microbiota depends majorly on the food habits of the people [9]. In a final word, the severity and exposure of respiratory infections caused by viruses like SARS-CoV2 may be influenced by the gut and lung microbiota diversity and it is closely related to our food source and diet patterns. Nowadays, probiotics are renowned health supplements that are pillars of our immune system and helps us to fight different diseases and infections[11–13]. These probiotics are live microorganisms (MOs), bacteria, or yeast, when ingested in adequate amounts confer a health benefit to the host [14,15]. The diet that is associated with health benefiting probiotics improves immunity and protects from the different infectious diseases through immunomodulation [16].

The current review speaks about probiotics as a therapy in this COVID-19 pandemic to reduce the chances of infection by improving the immune system. we have also discussed the role of diet for gut microbiota induced immunity.

Diet-Induced Microbiota Profile and Immunity

The human gastrointestinal tract (GI tract) is the site of focus where many kinds of reactions occur. However, recent discoveries have made it possible to answer the questions of how and why the GI tract is the focus of these reactions. The Human GI tract lining consists of trillion cells of MOs such as bacteria, yeast, and archaea that form a complex microbial community called the gut microbiome. The gut microbiome plays a vital role in digestion, fermentation of complex dietary compounds which are indigestible to humans, protect from virulent pathogens, acting as producers of vitamins, neurotransmitters, maintaining human health by modulating host immunity, production of signalling molecules such as cytokines, maturation of immune system, etc [17–23]. Belkacem et al. reported the administration of *Lactobacillus paracasei* and *L. plantarum* in the GI tract modulated immune system via regulating cytokine secretion and increasing immune cells in the lungs such as natural killer cells, macrophages and dendritic cells in influenza virus infection [24]. However, the balance of gut microbiota profile is of utmost importance as it plays a crucial role in maintaining human health throughout the life of an individual, and also, they are vital in providing the first line of defence [25–27]. The gut microbiome

seems to be very sensitive and does often change into several extrinsic and intrinsic factors such as genetics, dietary habits, age, geographic location, and ethnicity [26,28,29]. Amongst the above-mentioned factors, dietary habit seems to affect the gut microbiome with a huge impact that is substantially observed from the research studies [30–36].

In the Eastern diet, the key meals are lunch and dinner, typically made up of basics such as rice or pasta, chilli, and some vegetables and meat dishes [37]. South Asia harbours 26% of the world's population in the Eastern zone that houses tremendous genetic and cultural diversity residing in India as the largest country with a denser population [38–40]. Indians more often consume plant-based diets as per the studies conducted on gut and lung microbial profile, and effectiveness in immunity against various viruses. The data showed that Firmicutes and Actinobacteria specifically *Bifidobacterium* and *Lactobacillus,* play an important role in the stimulation of immune response against viruses. The high prevalence of Firmicutes that contains bacteria are responsible for fermentation and produces short-chain fatty acids (SCFA), these fatty acids fuels colonic epithelium thereby maintaining the integrity of epithelial cells, influencing metabolism and aiding in epithelial restitution which may be responsible to induce antigen-specific immune response [41]. A phylum-level study from Tandon et al. 2018 reported from a cohort of 80 Indians residing in the urban area that the gut microbiome of these individuals was rich in Bacteroidetes (71.5%) followed by Firmicutes (18.7%), Proteobacteria (3.8%), and Actinobacteria (0.6%), occupying majorly 5 genera *viz*., *Prevotella, Faecalibacterium, Alloprevotella, Roseburia,* and *Bacteroides* with more than 80% of abundance. The typical diet reported in these people of the urban area was simple and complex carbohydrates such as rice, wheat, sorghum, and fibre rich components majorly fruits, vegetables, sprouts, etc [42]. Contradictory to urban diet, tribal diet and rural diet show a much more balanced microbiome with the dominance of Firmicutes, followed by Proteobacteria, Bacteroidetes and Actinobacteria studied in south India. Tribal communities with this type of microbiome possessed a mixed diet rich in cereal millets such as pearl and finger millets along with moderate consumption of meat but did not consume milk or milk products. While rural diet used to be rich in rice and lentils along with milk, curd, and meat. At genus level, bacteria such as *Clostridium* (32.7% in tribal; 4.7% in rural) and *Bacteroidetes* (2.6% in tribal; 0.4% in rural) were abundant in tribal population than rural counterparts. While *Streptococcus* (0.4% in tribal; 2.7% in rural) and *Enterobacteriaceae* (0.4% in tribal; 1.2% in rural) were shown to be more prevalent in rural groups than in a tribal group. The study also stated an abundance of Firmicutes to an extent of 85.9% in tribal while 63.5% in the rural group [43]. The change in dietary pattern and lifestyle among tribal, rural, and urban has a direct correlation with gut microbiota. The tribal, as well as rural cohorts, were found to be rich in microbial diversity aspects owing to their high fibre intake whereas less diverse in urban groups owing to the modern dietary lifestyle. However, urban individuals microbial profile reveals an abundance of Bacteroidetes phyla and low dominance of Firmicutes when compared to rural and tribal populations [44–46]. The Western zone of the world mainly covers the American and European populations where they follow a similar pattern diet. Most Western populations consume overly processed and omnivorous foods with low dietary content, high in animal protein, total and saturated fats, and simple sugars [31,47].

The European diet resembles the Paleolithic age ancestors that include intake of vegetables, fruit, nuts, eggs, fish, lean meat while on the other hand excluding grains and dairy products [48,49]. A recent study regarding the modern Paleolithic diet (MPD) by Barone et al (2019) was performed on participants from urban areas of Italy where they obtained, 51.02% of energy from fats, 30.14% from proteins, and 18.84% from carbohydrates. Further, the dominance of asaccharolytic bacteria such as *Sutterella* and opportunistic pathogens such as *Odoribacter, Bilophila* was reported. The abundance of these pathogens can be traced back to their diet which is rich in animal proteins and high consumption of saturated fats. As well as there was the presence of *Akkermansia* which is considered as potential next-generation probiotics i.e. directly correlated to consumption of unsaturated fats. Finally, the study reported the dominance of Firmicutes followed by Bacteroidetes, Proteobacteria, Actinobacteria, and Verrucomicrobia at the phyla level [50]. Yet, the high

diet supports the more growth of the Firmicutes but it hampers the microbial diversity and thus compromises the gut induced immunity.

The standard American diet comprises of consumption of refined carbohydrates, fatty meats, and added fats that lack many nutrients in grains, fruits, and vegetables. Studies show that this type of dietary pattern contributes to various chronic diseases [51–53]. Furthermore, Americans follow a lavish diet to obtain 57.9% energy from ultra-processed foods involving sugar as well. The content of added sugar in these foods is usually eight-fold higher than in normally processed foods [54]. American population shows the loss of microbial diversity to a greater extent when compared to the ancestral population of Hadza tribes. In the American group, the high abundance of *Akkermansia muciniphila* and Bacteroides were found compared to the Hadza tribes community [55]. A study by David et al (2014) reported an increased abundance of *Alistipes putredinis, Bilophila Wadsworth*, *Bacteroides* sp. Along with genus Prevotella, phyla Bacteroidetes and Verrucomicrobia with a simultaneous decrease in the levels of Firmicutes resulting in reduced production of SCFAs [56]. Due to the high-fat diet, and processed foods there are higher microbial counts of mucus degrading microbes in the American population that may result in a higher risk of infections and diseases. Lower levels of Firmicutes and Bifidobacteria are also stated in these individuals with a heavy loss of microbial diversity and functionality. Based upon the various findings, it looks like that, reduction in health-promoting groups of Firmicutes and Actinobacteria count may reduce the immunity driven by the gut microbiota profile.

The Lung Microbiome

A vast variety of microbial communities inhabits the human body that is found to be more prevalent on mucous membranes and play a vital role in various metabolic processes [57]. Historically, the lungs were thought to be sterile and free from any microbial contact, yet it is constantly exposed to microbiota through inhalation. From the past decade, studies helped to understand how lung and microbiota interact and exist together [58,59]. In comparison with gastrointestinal microbiota, lung microbiota hosts relatively lower microbial communities that range from 4.5 to 8.25 log CFU/ml as the lung hosts low nutrients than the intestinal tract [60–62]. Several studies have been conducted to explore the healthy lung microbiome that comprises of two main phyla Bacteroidetes and Firmicutes [63,64]. However, other studies also postulated the dominance of phyla such as Proteobacteria, Actinobacteria, and Fusobacterium along with a relative abundance of Firmicutes and Bacteroidetes [60,62,65–67]. A genus-level study by Erb-Downward *et al.* (2011) showed a dominance of *Pseudomonas, Streptococcus, Prevotella, Fusobacterium, Haemophilus,* and *Porphyromonas* in the lower respiratory tract of healthy individuals [60]. Others reported a lower abundance of genera*, Veillonella, Leptotirchia,* while an ample amount of *Lactobacillus* and *Rothia* [68].

The healthy lung microbiome is sensitive to factors such as oxygen tension, blood flow, luminal pH, temperature, inflammation, allergen, and more precisely to the pathogenic MOs that may result in respiratory ailments and disorders [69,70]. The majority of respiratory infections are airborne which are caused by MOs that can travel and escape from mucosal and ciliary activity of epithelial cells present in the upper respiratory tract and adhere to the epithelial lining of the lower respiratory tract and profoundly multiple in lung alveoli. The result of infection would provoke immune-stimulating responses stimulating the respiratory microbiome to play a part in the prevention of respiratory infections [71–74].

Chronic obstructive pulmonary disease (COPD) is a group of respiratory diseases that are characterized by chronic obstruction of lung airflow which interferes with normal breathing. Many scientists have analyzed the lung microbiome of COPD patients and observed a lower bacterial diversity when compared to healthy populations [62]. At the genus level, the relative abundance of *Pseudomonas* was found which is one of the known opportunistic pathogens [65]. A similar study was stated by Huang *et al.* (2014) in COPD patients that observed enrichment of Proteobacteria *viz.* Moraxellaceae, Patuerellaceae, Pseudomonadaceae, and Enterobacteriaceae and concomitant reduction in the levels of Actinobacteria, Clostridia, and Bacteroidia [75]. ARI also show similar microbial signatures as that of COPD patient with an enriched microbiota of *Moraxella, Streptococcus,* and *Haemophilus*

[76]. Pneumonia is characterized by flooding of fluid in the alveoli of lungs that contains enough nutrients and creates oxygen barrier conditions, hence impairing its clearance by ciliary action of epithelial cells and thereby facilitating the growth of the microbial community with the dominance of pathogen, progressing the disease [73,77]. Recent data suggest a reduction in the pulmonary microbial diversity and reduction in *Rothia*, *Lactobacillus,* and *Streptococcus* which increases the risk of pneumonia, predominantly in the nasal mucosal lining [68]. Additionally, patients with HIV in later stages showed dysbiosis in respiratory microbiota with an increase in Prevotella and Veillonella group amidst the treatment and this microbial signature persists for years [78].

Thus, it seems that a healthy lung microbiome responsible for the normal function of lungs, generally habitats the dominance of phyla such as Proteobacteria and Fusobacterium along with a relative abundance of Firmicutes and Bacteroidetes with a higher abundance of *Lactobacillus*. Phyla such as Proteobacteria and Fusobacterium are generally responsible to initiate a pro-inflammatory immune response that leads to the severity of the disease while on the other hand, *Lactobacillus* genera modulate the immune response by activation of T_{reg} cells. These MOs are evidenced to play an important role in different respiratory diseases by creating an immunological barrier.

The Gut-Lung Axis

The gastrointestinal microbiota can modulate lung microbiota majorly through the impact of microbial metabolites produced by the gut microbiome. Dysbiosis in the gut is found to be linked with various diseases and respiratory infections are one of them [79,80]. One study has reported a decrease in the density of *Bifidobacteria* while a simultaneous increase in *Clostridia* in the intestine is associated with asthma [81]. Another research showed that the influenza virus infection in the respiratory tract significantly increased the count of Enterobacteriaceae with a concomitant reduction in *Lactobacilli* as well as *Lactococcus* levels were seen in gut microbiota [82]. Furthermore, depletion in microbial diversity by antibiotics in the gut increased the infection rate of influenza virus infection in the lungs when studied in a mouse model [82,83]. these findings corroborate that the gastrointestinal tract and lung are intensively linked organs that influence each other's homeostasis.

Role of Probiotics in Viral Infections

The human lungs have been adapted and improved the protection mechanisms from last hundreds of years to fight the invading infective viruses using the first line of defence system *viz.* mucus induction, continuous motion of cilia, nonspecific inhibitors for viral replications, secretion of Immunoglobulin A (IgA) in respiratory tract infections, etc. [84]. On the onset of a viral infection, a cascade starts that activates the body's natural immune mechanism. Initially, Toll-like receptors (TLRs) mediate the antiviral immune responses by recognizing virus infection, activate the signalling pathway leading to the secretion of chemokines and cytokines such as interferons (IFN) type I. Chemokines activate the natural killer cells (NK cells) that result in disruption of viral RNA and stop replication. Furthermore, the dendritic cells (DCs) lead to an activation of CD4+ and CD8+ cells and develop antigen-specific T and B lymphocytes mediated immunity that works together to get rid of the invading infective stage [85]. Microflora other than the digestive system, particularly in the lungs is also established to fight the incurring viral infections by modifying and supporting the natural immune process called immunomodulation. MOs and their secreted metabolites interact with TLRs, IFN, DCs, and T regulatory lymphocytes along with other chemokines and cytokines which is responsible to induce host immunity [83]. Human microflora plays a key role to support innate and adaptive immunity whereas probiotics are proven to stimulate host immunity via immunomodulation of the immune system. These probiotic microbes translate the innate immunity and induce the acquired immunity that results in stimulation of specific and non-specific immunity [86,87]

There are reports that probiotics such as *Bifidobacterium breve* shows anti-influenza effect by increasing the production of IgA, and IgG [88]. Hepatitis A and B were found to be reduced by *Lactobacillus acidophilus* and *Bifidobacterium bifidum* while *Thermophilus sp.* is known to work as an anti-herpetic agent [89,90]. Similarly, *Bifidobacterium lactis* and *Saccharomyces boulardii* can be used in antiviral therapy against Rotavirus [91]. A clinical study has reported that daily

consumption of probiotics by HIV infected people showed improvement of CD4+ count [92]. It is also suggested that the consumption of probiotics like LAB and *Bifidobacteria* are found to reduce the risk of upper respiratory tract infections [93]. An animal study demonstrated that oral administration of probiotic strains like *Lactobacillus pentosus, L. casei, L. plantarum, L. bulgaricus, L. rhamnosus, L. gasseri, L. brevis,* and *B.breve* helped to suppress symptoms of virus infection [94].

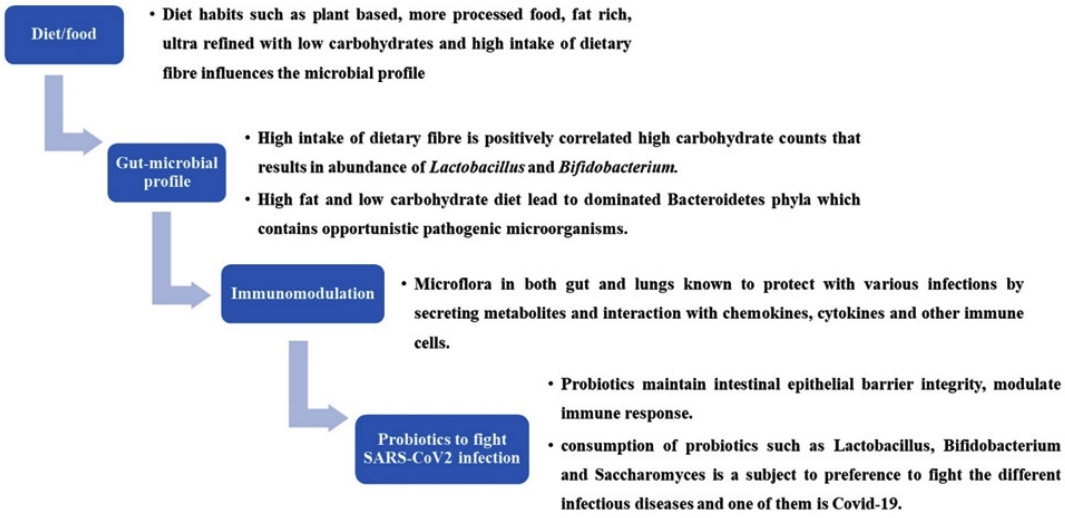

Fig. 1. Process of probiotic and immunomodulatory activity

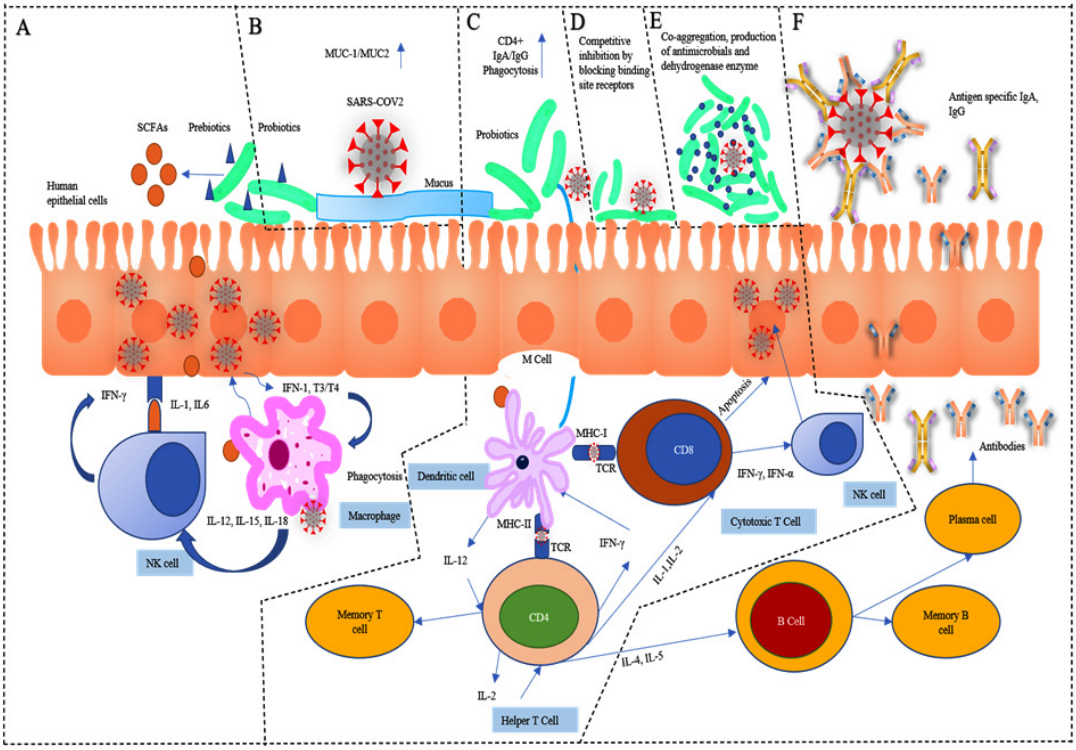

Fig. 2. Role of probiotics along with prebiotics in immunomodulatory

Table 1. List of microorganisms showing various immunological functions

Microorganisms	Functions	References
Bifidobacterium breve	Increases the production of IgA and IgG for anti-influenza effect	88
Lactobacillus acidophilus, Bifidobacterium bifidum Thermophilus sp	Improved hepatitis A and B.	89,90.
Bifidobacterium lactis, Saccharomyces boulardii	Improvement of CD4+ count	91,92
L. pentosus, L. casei, L. plantarum, L. bulgaricus, L. rhamnosus, L. gasseri, L. brevis, and *B.breve*	Help to suppress symptoms of virus infection	94
Lactobacillus and Bifidobacterium	Modulates the regulation of the immune system by cytokines, IgA and IgG production	108
L. rhamnosus and B. lactis	Increase IFN-α, IL-4, IL-10, and IL-6 in bronchoalveolar lavage	94
L. plantarum and L. reuteri	Reduce inflammatory parameters	
Probiotic MOs	Produce SCFAs and induce PRR by activating TNF-α	106,107
L. lactis, L. acidophilus	Antigen-specific immune response, increase Th1 cytokines, such as IL-2, IL-12, and IFN-α.	
L. Plantarum, L. reuteri	Improvement against pneumonia viral lethal infection	110
L. acidophilus, L. casei and L. bulgaricus	Production of IgG antibodies	110
Bifidobacterium bifidum, B. breve	Increase humoral immune response	
L. rhamnosus	Against rotavirus, leads to stimulate IL-4	114
L. casei, L. acidophilus	Induce IL-10 and CD4+ and T regulatory cells	109
L. acidophilus, L. casei, L. rhamnosus, L. helveticus	Enhance phagocytosis, cytokines and immunoglobulin production	86
Lactobacillus and Bifidobacterium longum mediated toll-like receptors	Stimulate TNF-α, IL-10, IL-12 also modulate T helper cell response in the gut and lung	16

Anticipation of the Immunomodulatory Role of Probiotics in SARS Cov2 Infection

Yet, no direct relation and study are available to justify the role of probiotics against SARS-CoV2 infections but many previous studies regarding probiotics and viral infections can be used to implement the possible mechanisms and their role [95,96]. The pathogenesis of SARS-CoV and SARS-CoV2 relied on a common entry point by interacting with the ACE2 receptor present on epithelial cell surfaces in the lung and intestine [97–100]. In the certain report of SARS-CoV2 infection, it has been postulated a dysbiotic condition caused by *Salmonella enterica*, a member of Enterobacteriaceae family was found abundant that increased the level of ACE2 receptors in the epithelial cells of the intestine resulting it to be more prone to get infected from these viruses [97]. The SARS-CoV2 virus has to surpass the immunologic barrier of respiratory tract epithelial to invade the cells through the ACE2 receptors whereas the probiotic microbes with commensal bacteria may help the immune system to reduce or inhibit this infection through immunomodulation [101,102].

Although, probiotics do not show a direct effect it creates an immunologic barrier by stimulating an immune response that supports the first line of defence of the body [103]. Generally, the probiotics interact with lung and intestinal epithelial as well as specialized cells (M cells) for immunoregulation through interaction with macrophages and dendritic cells which leads to activation of T and B lymphocytes. It may hamper the viral attachment by competitive inhibition via blocking the binding sites on the epithelial lining. The probiotics induce the upregulation of mucin-1 (MUC1) and mucin-2 (MUC2) that can also prevent attachment of the virus to an epithelial cell and suppress the replication. Finally, it also produces antimicrobial peptides and dehydrogenase and nuclease enzymes which can break down the viral nucleic acid, and also the co-aggregation of probiotics with viral particles interferes with the attachment of the virus to the epithelial cell line [104]. Probiotics also have a significant role in the induction of type 1 T helper (Th1) cell which is specific for antimicrobial/antiviral mediated immunity whereas IFN which is a glycoprotein and IgA are considered antiviral agents [16,105]. One of the important molecules produced by probiotic MOs by breaking down the prebiotic compound is short-chain SCFA. It influences the immune system and induces pattern recognition receptors (PRR) by activating tumour necrosis factor- á (TNF-á) [106,107]. More precisely, probiotics like *Lactobacillus* and *Bifidobacterium* modulates the immune system by regulating the cytokines, increasing the production of IgA and IgG antibodies [108]. Specifically, the *Lactobacillus* species like *L. acidophilus, L. casei, L. rhamnosus, L. helveticus* are effective to enhance phagocytosis and improve the secretion of cytokines, immunoglobulin and plasma cells, as shown in a study, *L. casei* and *L. acidophilus* induced the interleukin (IL) such as IL-10 and CD4+ regulatory T (Treg) cells (Susan and Terry, 2009, Markowiak and Œli¿ewska, 2017). Moreover, the administration of *L. plantarum* and *L. reuteri* reduced inflammation while *L. rhamnosus* and *B. lactis* increased IFN-ã, IL-4, IL-10, and IL-6 in bronchoalveolar lavage [94]. Besides, probiotics can induce the level of Bcl2 (B cell lymphoma 2), which is responsible for the activation of cellular and humoral immunity leading to the activation and production of the cytokines along with Th1/Th2 expression.

Probiotics have also been studied for their influence on immune-related gene expression and activation of cytokines, depending on the contact-based mechanism. A study suggested that probiotics like *Lactobacillus* mediates the expression of TLR2 which stimulates TNF-á while *Bifidobacterium longum* mediated expression of IL-10 and IL-12 via a contact-based mechanism that resulted in the modulation of T helper cell response in the gut and lung [109].

The oral administration of 10^9 CFU of probiotics are known to be more effective that may exert long term homeostasis and immunomodulatory effect on the host [110,111]. Oral administration of *Bifidobacterium bifidum* and *B. breve* have also been shown to increase humoral immune response such as stimulation of IgA [111]. Thus, probiotics also show the possibility to use as a live vaccine for oral immunization. Moeini et al. (2011) used *L. acidophilus* as a live vehicle for oral immunization against chicken anemia virus (CAV). The AcmA-binding domains present on the surface of *Lactococcus lactis* were used to display the viral protein 1 (VP1) CAV on *L.*

acidophilus to immunize specific-pathogen-free chickens through the oral route. The immunization increased the levels of Th1 cytokines, such as IL-2, IL-12, and IFN-ã [112]. Furthermore, some studies have shown that probiotics can enhance the outcome of influenza virus infection when administered through the nasal pathway. The nasal administration of *Lactobacillus rhamnosus* strains CRL1505 and CRL1506 were able to improve respiratory antiviral defences and beneficially modulated the immune response by triggering the TLR3 and PRR (RIG-I, a retinoic acid-inducible gene I) against the respiratory syncytial virus (RSV) [113].

It has been now clear that probiotics are microbiota that works as a potential barrier in the case of any viral attack through immunomodulation as described earlier (Figure 1). It may act indirectly through competitive inhibition or directly via the interaction of immune cells by producing chemokines, cytokines, and also be involved in other immunologic pathways. In light of this information, we can anticipate the possible role of these probiotics in the protection or reduction of the SARS-CoV2 infection. In this context, a model has been represented here showing the expected immunomodulatory role of probiotics along with prebiotics which may take place on the onset of SARS-CoV2 infection in a more or less similar way (Figure 2) (Table 1).

CONCLUSIONS

Various studies have proven the role of dietary habits in determining the gut-microbiota profile and its likeliness to fight different viral infections. It has been shown that change in dietary pattern and lifestyle among tribal, rural, and urban has a direct correlation with gut microbiota. Specifically, the diet habits impart a direct role in the ratio of Bacteroidetes and Firmicutes in the gut that eventually participates in the immunomodulation activities against different diseases. These phyla encounter many probiotics genera which appear to be effective to maintain intestinal epithelial barrier integrity, modulating the immune response, and also directing the microbiota profile of the lung environment through the gut-lung axis. It is being correlated with the studies that diversity in microbial population in the gut provides may provide more immune response and lowers the risk of severe infections from SARS-CoV2. Thus, administration of probiotics such as *Lactobacillus, Bifidobacterium*, and *Saccharomyces* are subject to preference to fight the Covid-19 infection.

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Conflict of Interest

The authors declared no conflict of interests.

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