*Review*

# Potential role of microbiota in the prevention and therapeutic management of infectious diseases

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**Abstract:** A huge diversity of microbial species continues to live with the human beings that are collectively known as microbiota. Several environmental factors can impact the microbial imbalance in the intestine which can play a starring role in health and disease conditions in humans. In this review, we have described the role of human microbiota in the individual's susceptibility to infectious diseases such as gastrointestinal, respiratory, and female reproductive tract infections. Here, we have discussed how the indigenous microbiota interacts with the host and the invader microorganisms including bacteria, fungi, and viruses, and can modify the outcome of infections. The complex mechanisms of colonization resistance mediated by the microbiota as a direct and indirect way to fight against the infectious agents have been highlighted. Moreover, the approaches for the modulation of human microbiota for the prevention or therapeutic management of infectious diseases have been discussed especially the potential therapies directly targeting the microbiota such as probiotics, prebiotics, as well as fecal microbiota transplantation. Further studies need to focus on the complex interactions between the host and microbial species which could be helpful for a better understanding of the hidden potential of gut microbiota in the physiology of the host and could provide novel therapeutic targets and approaches.

**Keywords:** Colonization; Microbiota; Infections; Probiotics; Synbiotics

## 1. Introduction

The normal flora of humans is composed of viruses, archaea, bacteria, parasites, and fungi. Among these microbes, bacteria are abundantly present in different parts of the human body such as the skin, nasal cavity, oral cavity, intestine, and genitourinary system [1]. It has been reported that gut microbiota has approximately 1013 to 1014 microbial diversity which is estimated from the number of bacterial cells present in the colon (habitat of the largest number of microbial cells) [2]. Three major classes of bacteria i.e., Actinobacteria, Bacteroidetes, and Firmicutes plays role in the composition of gut microbiota. Recent studies have provided strong evidence that gut microbiota is a potential controller of human health as well as diseases. Gut microbiota is responsible for many important functions such as the maintenance of hemostasis, immunomodulation, and drug metabolism [3]. The interactions of microbiota with the host, the composition of the microbiota,

as well as characteristics of the human microbiome are not clearly understood due to limited research

It has been thought that several environmental and genetic factors affect the human microbiome, but further research is needed to reveal the causes of microbiota-associated diseases and the link between gut microbiota and human health [4]. Results of different reported studies indicated that several factors such as diet, antibiotic treatment, and gene polymorphism affect the composition of the microbiota. Different physiological, anatomical, and mechanical barriers protect the mucosal surfaces (genitourinary and respiratory tract). Pathogens cause infection in the host by disrupting these mucosal surfaces. On the other hand, a protective mechanism known as colonization resistance exist in which colonization of bacteria pathogens (which disrupt the microbiota and cause virulent diseases) is prevented. Normally, a symbiotic relationship between gut microbiota and host exists in which nutrients, as well as optimum growth conditions, are provided to microbiota via the host, whereas microbiota helps in angiogenesis, the development of the immune system, and the storage of fats in the host cell [3,4]. It has been thought that maintenance of the dense population of microbiota and inhibition to colonize the bacterial pathogens is due to the symbiosis, but the underlying mechanism of colonization resistance is still elusive. Despite these protective barriers and prohibition of colonization, still few pathogens are responsible to cause infection in the gut, but the mechanism by which these pathogens disturb these barriers and affect the intrinsic microbiota is poorly understood. Recently, studies showed that *Citrobacter* spp and *S.* Typhimurium are enteric pathogens and cause inflammation in the gut which results in altering the composition of the microbiota and providing optimum growth conditions [5]. The bacterial microbiota is particularly important in the commonest respiratory and gastrointestinal infections especially necrotizing enterocolitis and *Clostridium difficile* infections (CDIs) [6].

Certainly, the studies shed light on the significance of microflora, however, the research is at its initial stage, and the findings are increasingly filling the knowledge gap, especially in host-microbiome relationships and their implications in the pathogenesis and therapeutic value of some diseases. Here we have discussed the recent studies particularly related to the role of gut microbiome dysbiosis in certain human disorders. Moreover, the microbiome-based therapeutic approaches to the specific disease conditions for the restoration of health have been discussed.

## 2. Human microbiota and its diverse functions

The human microbiota is composed of different microbes including archaea, viruses, protozoa, and mainly bacteria which inhabit different parts of the human body for example in GIT, reproductive organs, skin, oral cavity, and the respiratory tract [1]. Three major phyla including Actinobacteria, Firmicutes, and Bacteroidetes primarily colonized human GIT microbiota [7]. Different pathways including neuroendocrine, metabolic, and immune interactions are helpful in the regulation and stabilization of the relationship between host and intestinal microbiota.

### 2.1. Metabolism

An important function of gut microbiota is in the digestion of a fiber-containing diet and unabsorbed starch. The end product of such food is in the form of short-chain fatty acids including acetate, pentanoate, propionate, and butyrate, these short-chain fatty acids provide 10% extra energy to the host to perform other metabolic processes efficiently [8]. Furthermore, in the colon, short-chain fatty acids produced by bacteria provide 70% of the total energy that's why butyrate is termed as fuel for cells of the colon [9]. In GF mice, it was observed that microorganisms that produce butyrate may inhibit the lower rates of ATP synthesis, mitochondrial respiration, and autophagy in the cells of the large intestine which shows that butyrate plays role in ATP production [9]. On the other hand, species of intestinal microbiota, for example, *Enterobacter agglomerans*, *Bacteroides fragilis*, *Enterococcus faecium*, *Eubacterium lentum*, and *Serratia marcescens* play a key role in the

synthesis of vitamin K2 (also known as menaquinone) which reduces the level of cholesterol and high-density lipoproteins (HDL) which helps in the prevention of cardiovascular diseases [10]. Intestinal microbiota also synthesizes vitamin B for hosts commonly B12 and B5, both of them produce two major neurohormones i.e. cortisol and acetylcholine which perform the normal function of the brain [11]. The deficiency of these vitamins is associated with various diseases including insomnia, and hematological and psychological disorders [12]. Bile salts play role in the digestion of fats and lipids by combining with glycine or taurine, at first, these bile salts are stored in the gall bladder and then secreted to the duodenum where digestion takes place, which shows that intestinal microbiota helps in the co-metabolism of cholesterol derivatives. They have antibacterial activities that prevent the growth and development of microorganisms that are resistant to bile acids, by the modulation of the integrity of bacterial cell membrane which results in the leakage of cellular contents [13]. Furthermore, intestinal microbiota helps in the absorption of several compounds such as phenolic compounds (such as flavonoids, lignans, tannins, etc.) that are present in fruits, vegetables, and the derivative of plants, among them, the metabolism of flavonoids takes place in the small intestine.

*2.2. Microbiota, immune and nervous system: A triad*

The intestinal barrier has various proteins that play a key role in the regulation and permeability of the cell. The composition of the intestinal barrier includes epithelial and mucus lining which acts as a bridge between the outer world and the internal environment of the host.   Disruption in the function of this barrier may result in enhanced intestinal permeability to the derivatives of microbes, commensal microbes, and other luminal components, which elicit immune responses by abrupt functioning of T cells and molecular imitation and causes immune-mediated disorders such as allergy, inflammation as well as autoimmune diseases [14]. The interaction between host and gut microbiota helps in the cross-regulation of the function of both immune-mediated and physical barriers. It has been reported that short-chain fatty acids protect the GI barrier against the harmful effects of proinflammatory cytokines, the underlying mechanism by which they confer protection is still unknown [15]. Furthermore, it is suggested that short-chain fatty acids help in the functioning and development of microglial cells [16]. On the other hand, the community of microbes that colonize the gut provokes both humoral and cell-mediated immunity. Cells of the innate immune system (hematopoietic as well as non-hematopoietic cells) recognize microbial-derived products and signals   [17]. In vivo study, healthy mice were compared with germ-free mice which shows that germ-free mice have an abnormal growth of lymphoid tissues as well as antibody production. The studies have demonstrated that the tolerogenic response is mediated by the gut microbiota which acts on the dendritic cells of the intestine and reduces the T-helper cell 17 (Th17) pathway [18].

## 3. Human microbiota in health

The physiological functions of the host are significantly affected by intestinal micro-biota. The human body is colonized by different microorganisms such as prokaryotes (ar-chaea and bacteria), eukaryotes, and viruses. The human body is colonized by thousands of different known bacterial species as well as the diversity of bacterial genes. Several fac-tors such as diet, gender, age, and race affect the composition as well as the function of microbiota [19]. After birth, the host is colonized by the simple community of bacteria, furthermore during the growth of the host development of microbiota occurs gradually [20-22]. Over time host and bacterial association results in many useful functions, such as symbiosis, bacteria help in intestinal function, preventing the colonization of harmful bac-teria, and the digestion of some compounds [18,23]. Some foods are not metabolized by the stomach e.g., xyloglucans which are the primary diet fiber present in vegetables, in this case, species of gut microbiota significantly Bacteroides plays a role in the digestion [24]. However, some useful bacteria including Bifidobacterium and Lactobacillus use

other fibers that cannot be digested for example oligosaccharides and fructooligosaccharides [25]. Gut microbiota also plays a key role in the production of several vitamins and the maintenance of the homeostasis of lipids and proteins [26]. It has been estimated that intestinal microbiota yields approximately 100mmol/L SCFAs including butyric acid, acetic acid, and propionic acid per day, and provides energy to the gut epithelial cells. After absorption of these short-chain fatty acids in the large intestine, they perform several functions such as the homeostasis of glucose, energy harvesting, and the regulation of gut motility [27]. Microbes have both beneficial as well as harmful effects on human health.

It has been thought that human microbiota is useful in the disease alteration, in provoking immune responses, functional component, which is associated with alteration of antibiotic interactions, the modifier of genetic diversity, and in co-metabolism. Although, several diseases can be inhibited and treated by beneficial bacteria known as probiotics [28,29]. The human microbiome synthesizes many primary and secondary metabolites that have several possible applications, but the isolation, classification, and function of all metabolites are still unknown. With the help of primary gene sequencing from the human microbiome, antibiotics against MRSA (methicillin-resistant *Staphylococcus aureus*) were discovered [30]. On the other hand, the human microbiome regulates the body's functions and is helpful in the treatment of several gastrointestinal diseases including necrotizing enterocolitis, diarrhea, and IBD. In vivo study, it was observed when 17 strains of clostridia from human microbiota were given orally to the mice there was a significant decrease in both diseases i.e., colitis and diarrhea [31]. In infants, probiotics have potentially beneficial effects to treat some allergic diseases. Some microorganisms are also recognized as potential biomarkers in the identification of diseases [32].

## 4. Human microbiota in infectious diseases

Gut dysbiosis frequently causes a disease that is termed an infection. Whenever there is a disruption in the colonization of gut mucosa it results in the translocation of gut microbiota which causes inflammation [33]. Furthermore, it has been illustrated that infection and gut dysbiosis are closely related [34]. One study supported the notion that host response can be modulated by native microbiota which induces lower inflammatory responses which in turn causes increased chances to acquire the infection, for instance, patients having *Clostridium difficile* infection have different gut microbiota [35]. The gut microbiota is important in several infectious diseases as shown in Table 1.

### 4.1. Infection with Clostridium difficile

When broad-spectrum antibiotics are given to the patients there is abnormally increased growth of *Clostridium difficile* which is the cause of antibiotic-associated diarrhea [35]. *Clostridium difficile* is predominately present in the intestinal flora, which is gram-positive, strict anaerobe, and spore-forming bacteria. *Clostridium difficile* causes infection by the disruption of intestinal flora and homeostasis which in turn reduces the mechanism of colonization resistance against toxin-producing *Clostridium difficile*. It was observed that in response to the antibiotic administration, the bacterial diversity in stool is reduced with an overall shift in the microbial composition among those with CDI. Moreover, there is an increased number of microbes secreting endotoxin as well as phylotypes that secrete lactate and a lower number of anaerobic bacteria that secrete butyrate in such patients [35]. As compared to healthy controls, the level of anaerobic bacteria which produce butyrate is considerably decreased in patients receiving antibiotics which increases the risk of colonization of *Clostridium difficile*. In children, several strains of *Clostridium difficile* influence fecal microbiota in a different way. Toxin A and B positive strains of *Clostridium difficile* significantly decreased the fecal bacterial community as compared to its only toxin B-positive strains.

**Table 1.** The association between gut microbiome alteration and human diseases.

| Category | Disorders | Microbiota alteration | | References |
|---|---|---|---|---|
| | | **Increased** | **Decreased** | |
| Cancer | Colorectal cancer | *Bacteroides fragilis*, Campylobacter species, Fusobacterium | Faecalibacterium, Roseburia | [36] |
| Immune-mediated disorders | Atopic disease | *Clostridium difficile*, *Clostridium difficile*/Bifidobacteria ratio | - | [37] |
| | Celiac disease | Bacteroides | Bifidobacterium | [38,39] |
| | Diabetes (Type-1) | Bacteroidetes | Actinobacteria, Firmicutes, Firmicutes/Bacteroidetes ratio | [40] |
| | Inflammatory bowel disease | *Bacteroides fragilis*, Enterobacteriaceae species, *Ruminococcus* sp. | Firmicutes, Roseburia hominis | [41,42] |
| | Irritable bowel syndrome | Escherichia coli | Bifidobacterium, Clostridium leptum | [43] |
| | Rheumatoid arthritis | *Prevotella copri* | *Bacteroides* species | [44] |
| | Systemic lupus erythematosus | Blautia species, Proteobacteria. | *Alistipes* species, *Odoribacter* species | |
| Infectious diseases | *Clostridium difficile* infection | *Clostridium difficile* | *Clostridium scindens*, Overall gut microbiota diversity | [45] |
| Kidney diseases | Chronic kidney disease | Actinobacteria, Firmicutes, Proteobacteria, | Lactobacilli | [46] |
| Metabolic and related cardiovascular disorders | Diabetes (Type-2) | Lactobacillus | *Clostridium coccoides*, Prevotella | [47] |
| | Hypertension | Firmicutes/Bacteroidetes ratio | Overall microbiota diversity | [48] |
| | Obesity | Actinobacteria, Firmicutes | | [49] |
| Neuropsychiatric disorders | Autism spectrum disorder | Bacteroidetes, Clostridium species, Desulfovibrio, Lactobacillus | Bifidobacteria | [50,51] |

| Depression | Anaerofilum, Eggerthella, Holdemania, Paraprevotella, Turicibacter | Dialister, Prevotella, Overall gut microbiota diversity | [52] |
|---|---|---|---|
| Parkinson's Disease | Coprococcus, Blautia, Roseburia | - | [53] |

### 4.2. Infection with Helicobacter pylori

A bacterium that causes diseases in the stomach is termed Helicobacter pylori. It is also associated with the infection of gums such as periodontitis. It has been observed that H. pylori-infected individuals have an increased number of *Fusobacterium nucleatum*, *Treponema denticola*, *Porphyromonas gingivalis*, and *Prevotella intermedia* whereas the decreased number of *Aggregatibacter actinomycetemcomitans* [54]. Patients with *H. Pylori* infection have increased probing depth as well as attachment loss, furthermore, it causes the growth and development of periodontal pathogens and ultimately lead to chronic periodontitis [54].

### 4.3. Bacterial vaginosis

Bacterial vaginosis has harmful effects on human health, for example, premature birth and individuals are at higher risk of having STIs (sexually transmitted infections). The vaginal microbiota is composed of a higher ratio of anaerobes, such as Gardnerella, Prevotella, Sneathia, Atopobium, Megasphaera, and Dialister whereas a lower number of Lactobacillus species [55]. Due to a higher ratio of colonization of these microorganisms, there is a higher risk of acquiring bacterial vaginosis and other STIs (sexually transmitted infections) such as acquired immunodeficiency syndrome (AIDS), and pelvic inflammatory disease (PID), and human papilloma viral infections. Bacterial vaginosis is the possible cause of inflammation of the female reproductive tract. Recently, scientists found the microbial community which causes bacterial vaginosis and other inflammatory diseases [56].

### 4.4. Infection with HIV

HIV is considered a global health concern currently, HIV patients have disrupted functions of intestinal microbiota furthermore, it has been seen that HIV-1 patients have a larger number of Bacteroidetes and Firmicutes [57]. After HAART (highly active antiretroviral therapy) viral loads in HIV-1 patients were significantly decreased, but it does not affect dysbiosis [57]. A study in South Africa has reported that young women and girls under 20 years of age are at higher risk to acquire HIV infection due to several biological factors. When microbiota of the vagina of these women was keenly observed, Cohen found another microbe Gardnerella, which showed that HIV infection is associated with the vaginal microbiome [34]. However, Gardnerella attacks antiviral drugs specifically tenofovir which fails tenofovir treatment [34]. Another study proved that microorganisms present in the vagina also affect the rate of HIV for example, *Prevotella bivia* a microbe present in the vagina causes inflammation.

## 5. Interaction among host, microbiota, and pathogens

The interaction between microbes, host, and intestinal microbiota can be followed by health as well as a disease [58]. Colonization resistance control this interaction which can be maintained by intestinal microflora directly or indirectly. In direct mechanism, native microbiota prevents the growth of foreign microbes directly by different processes, for example, a change in composition and function of the microbial community can lead to the disruption of the balance between the host and the microbiota, and consequently, infection occurs. On the other hand, in the indirect mechanism of colonization resistance,

microbiota evokes mucosal immune responses of the host and inhibits the entry of pathogen and infection. Furthermore, native microbiota affects both the responses as well as the development of the mucosal immune system [18].

## 6. The microbiota inhibits the colonization of harmful bacterial pathogens

Intestinal microbiota plays a crucial role in the colonization resistance in which microbiota protects the host against the colonization of harmful microbes as well as inhibits the growth of infectious microbes that confer infection. Several factors influence the function as well as the structure of human microbiota, for instance, antibiotics mediate the growth, persistence, and colonization of microorganisms. When there is an overgrowth of the microbial community, they interact with host cells to cause infection via direct contact with the epithelium of host cells or through secreted products. To understand the mechanism of how they protect the host cell from the invasion of microbes, principles of community ecology can be used [59]. Several factors affect the survival of the invading bacterial species in any established population and rate of growth, for example, environment (physical), available resources, natural enemies, and niche availability [60].

For example, in the pathogenesis of CDI, a niche opportunity plays an important role. To mediate colonization in patients that were given the antibiotics *Clostridium difficile* exploits the nutrient availability of hosts. The niche can also be formed by antibiotics through the modulation of bile acid metabolism. The route of transmission of *Clostridium difficile* is through spores in which to produce active vegetative cells specific bile acid signals are involved. Different studies suggested that the use of antibiotics results in a decrease in the microbes having 7$\alpha$-dehydroxylase activity, furthermore, it results in the decreased production of secondary bile acids (e.g., deoxycholate) which in turn causes elevated levels of primary bile acids (e.g., taurocholate). This phenomenon is significant because deoxycholate takes part to prevent *Clostridium difficile* growth, and taurocholate helps in spore germination. Furthermore, the germination of *Clostridium difficile* spores can be inhibited by using antibiotics that modify the deoxycholate concentration [61]. A mucosal immune system such as the physical barrier of the intestinal epithelium, antimicrobial peptides (AMPs) as well as the production of immunoglobulins regulates the relative abundance of the indigenous microbial species and response to the pathogenic challenges. Furthermore, when these processes do not take place pathogens have more chances to invade the human body and cause infection. Through the maintenance of homeostasis, intestinal microbiota prohibits pathogenic expansion. The mucus layer has several components among them most common are mucins which are composed of glycoproteins. Mucins are secreted within different parts such as the female genital tract, GIT, and respiratory tract [62]. Furthermore, the apical sides of the epithelium produce mucins inside the lumen. In vivo study, it has been observed that intestinal mucus act as a physical barrier and prevents the invasion of the pathogen, and animals that lack MUC2 have disrupted mucus lining allowing the pathogens to attach to host epithelium and ultimately leading to the inflammation of the colon [63]. The composition of earlier intestinal microbiota affects the production of mucin, for example, a decreased level of MUC2 was observed in GF mice. It is thought that different species of Bifidobacterium play a crucial role in the protection of the mucus layer [64]. Recently, a study was reported in which HIOs (human intestinal organoids) were used as a testing model to check the association between the development of gut microbiota and E. coli's colonization, which has shown that E. coli helps in the increased secretion of the intestinal epithelial mucins [65]. Furthermore, when *Clostridium difficile* was injected into human intestinal organoids the production of MUC2 was decreased and patients having *Clostridium difficile* infection had reduced production of MUC2 [66]. During infection, the composition of the intestinal microbiota can be modulated through diet and can lead to the degradation of mucin. Antimicrobial peptides are secreted by different cells such as neutrophils, adipocytes, epithelial cells, mast cells, and paneth cells, which are major elements of innate immune defenses. Antimicrobial peptides are produced at all mucosal surfaces and the constitution

of intestinal microbiota, as well as specific microbes, play role in increasing the expression of AMPs. [67]. Two other species *Bifidobacterium breve* and *Bacteroides thetaiotaomicron* help in the upregulation of REGIIIγ expression which prevents the growth of the gram-positive bacteria in the gut [68]. SCFAs (Short-chain fatty acids) are end products of bacterial fermentation which can change the AMPs production and provide energy to the cells of the colon, for instance, butyrate, acetate, and propionate are significantly present in the colon. Furthermore, SCFAs can also minimize the activity of microbes in the colon. It has been thought that lower concentrations of propionate can be used as a carbon source by Salmonella whereas higher concentrations hinder its growth [69]. The growth of *Salmonella typhimurium* can be inhibited by propionate by disturbing the mechanism of homeostasis within the cells [70]. In murine models, it was observed when a diet enriched with butyrate and propionate was given it reduced the bacterial activity which results in the decrease of *Clostridium difficile* infection which shows that short-chain fatty acids inhibit the CDI [71].

### 7. Treatment strategies to modulate microbiota

To inhibit colonization of microorganisms and their clearance several treatment strategies are used to modulate intestinal microbiota for example transplantation of fecal microbiota (FMT), probiotics, prebiotics, and synbiotics (Figure 1). In clinical settings, these strategies remain successful but the underlying mechanisms by which they act are not clearly understood.

### 7.1. Probiotics

It is considered that probiotics combat microbes for dietary as well as functional resources to inhibit recurrent infections. In the mice model, it has been seen, that spores of *Clostridium difficile* that are non-toxigenic can inhibit colonizing the toxigenic *Clostridium difficile* and can decrease the rate of infection significantly [72]. Furthermore, despite occupying a vacant niche, probiotics produce several antimicrobial constituents, for example, bacteriocins which play a role in the inhibition of microbial growth [73]. It has been observed that probiotics may work by blocking the adhesion of microbes to the epithelial cells of the host through direct interaction [74].

### 7.2. Prebiotics

To reduce the use of antibiotics in the treatment of infectious diseases and to minimize the rates of infection prebiotics are significantly used [75]. Prebiotics prohibit microbial growth by different mechanisms of action. For example, it has been observed that prebiotics is used in the promotion of growth of some species of predominant microbiota (*Bifidobacterium* species) in which prebiotics acts as a substrate for fermentation and breaks the bonds formed between fructooligosaccharide and galactooligosaccharide [76]. The prebiotics can result in the increase of targeted bacterial species within a particular community and inhibit the expansion of pathogens by niche exclusion. Prebiotics produce many fermentation products but among them, short-chain fatty acids are the major products [77]. Prebiotics acts through different mechanisms, for example, by inhibiting the growth of pathogens, by restoring secondary by-products of bacteria or bacterial metabolism e.g. salt metabolism or butyrate respectively, by decreasing the capability of the pathogen to adhere to the epithelium of the host by mimicking the ligands on host-cell receptors and short-chain fatty acids play role in the regulation of immune responses [70,71]. In vivo study, when healthy individuals were supplemented with resistant starch, the production of butyrate was significantly increased [78].
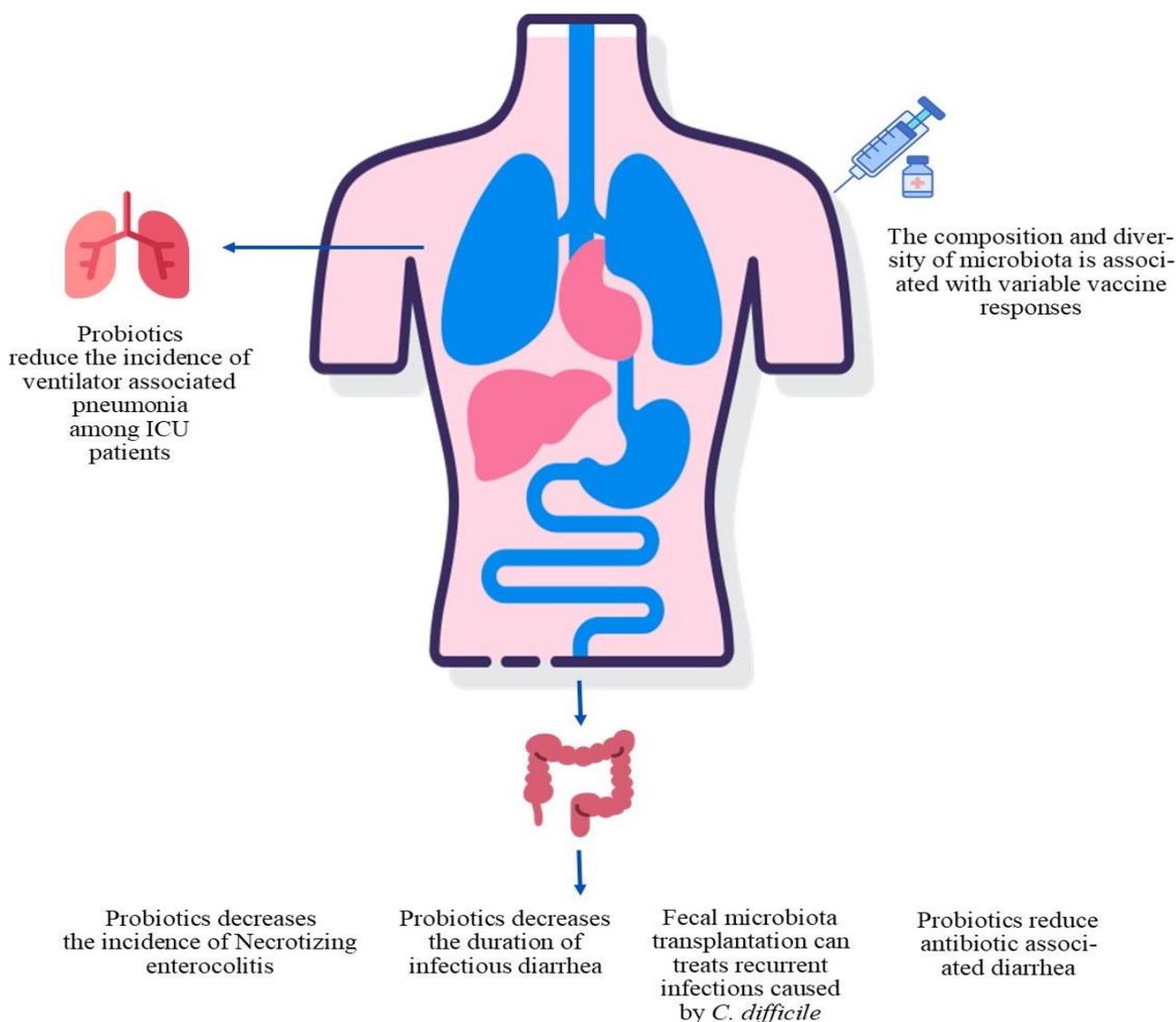
**Figure 1.** The therapeutic role of microbiome manipulation in the management of infectious diseases

### 7.3. Synbiotics

A combination of probiotics and prebiotics that works synergistically is called synbiotics. The sepsis may result in systemic inflammation causing increased rates of illness and ultimately deaths in infants. Treatment or preventive measures for sepsis are yet unavailable and millions of deaths of infants by sepsis occur every year [79]. Recently, in India to prevent sepsis efficiency of an oral synbiotic, consisting of fructooligosaccharide and *Lactobacillus plantarum*, was checked by a placebo-controlled, double-blind, and randomized trial [80]. Consequently, many infants that were administered with the synbiotic exhibited a significant decrease in morbidity and mortality rates. Furthermore, this synbiotic is now widely used for the treatment of neonatal sepsis, it costs only US$1 for seven days of treatment. It is cheap as well as has great efficiency.

### 7.4. Fecal microbiota transplantation (FMT)

To treat an infection or sometimes diseases the intestinal microbiota is modulated by fecal microbiota transplantation in which fecal suspension is transferred from healthy individuals to the patient. For the past few years, fecal microbiota transplantation is widely used for the treatment of *Clostridium difficile* infection. [81]. It has gained some

attention in the treatment of diseases caused by MDR organisms, for example, MDR *Staphylococcus aureus*, ESBL, vancomycin-resistant enterococci, and Enterobacteriaceae that produces carbapenemase [82]. The underlying process by which fecal microbiota transplantation acts is not properly known, but different studies have shown different processes. Recently, the virome of the patient having *Clostridium difficile* infection was observed before delivery of fecal suspension it has been observed that the patient has a disease with higher rates of Caudovirales bacteriophages as compared to healthy controls [83]. Consequently, positive clinical trials show that it modulates intestinal microbiota as well as enteric virome, and patients in which fecal suspension of a healthy individual was delivered exhibit lower rates of Caudovirales. FMT has a 90% success rate in individuals with CDIs, therefore, FMT was approved FDA for applications in the CDI. Some studies have reported that FMT could an efficient method for the treatment of IBDs including ulcerative colitis and Crohn's disease [84].

## 8. Conclusion and future prospects

The recent advancements in studying the dynamic, complex, and diverse microbial communities have helped us to understand the role of microbiota in homeostasis and susceptibility to infectious disease. It is understood that shifting the microbial community structures can alter its function which can ultimately be linked with susceptibility and outcomes for any particular infectious disease. Despite major improvements that have been made to understand the relationship between microbial species and infectious diseases, many questions remain unanswered. For the development of host immunity, the role of intestinal microbiota is evident. Further, it can protect the gut from invasion by the pathogenic microbes through colonization resistance and nutritional competition. Contrarily, infectious diseases result in the alterations of gut microbiota through altering intestinal function and immunomodulation. Whereas the alteration of the intestinal microbial population results in inflammation that may aggravate the course of infectious diseases. So far, the most valuable means for the regulation of gut microbiota is the use of probiotics that helps to prevent and manage infectious diseases. Moreover, recent studies have highlighted the potential of FMT in the management of certain infections. It is evident that infectious diseases are not limited to a single microorganism, therefore it is important to understand the intricate dynamics of microbial communities and hosts for better use of human microbiota in the prevention of infectious diseases with more refined treatment approaches.

**Conflicts of Interest:** The authors declare no conflict of interest.

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