



## Review Article

# Utilization of Probiotics in Treatment of Gastrointestinal Infections among Children

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## ARTICLE INFO

### Key Words:

Probiotics, Gastrointestinal Infections, Treatment, Children

### How to Cite:

Fatima, A., & Khan, S. . (2022). Utilization of Probiotics in Treatment of Gastrointestinal Infections among Children: Probiotics in Treatment of Gastrointestinal Infections among Children. *Pakistan BioMedical Journal*, 5(9). <https://doi.org/10.54393/pbmj.v5i9.786>

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Received Date: 25<sup>th</sup> August, 2022

Acceptance Date: 12<sup>th</sup> September, 2022

Published Date: 30<sup>th</sup> September, 2022

## ABSTRACT

Probiotics have been extensively studied and examined globally. Probiotics are extremely important for human health and encourage the growth of good bacteria in the human body. Probiotics exert its beneficial effect in the human body through a number of mechanisms, including the production of antibacterial chemicals, the eradication of pathogenic bacteria, and the prevention of the synthesis of toxic substances. Probiotics are now available in the market as functional foods and dietary supplements. The probiotics market is expected to increase from \$35.6 billion in 2015 to \$64.6 billion in 2023. Lactobacillus and Bifidobacteria are the most commonly used probiotics in the infant formulas. Probiotics are extremely beneficial for the gut health. Various factors disrupt the microflora of gastrointestinal tract of infants and cause various GI infections and diseases. **Methods:** Previous articles have been studied to develop this review article about a broad spectrum of pediatric disorders treated with probiotics. Probiotics are helpful in the prevention of irritable bowel syndrome, constipation, diarrhoea, gastrointestinal reflux disease, inflammatory bowel disease, acute gastroenteritis, infantile colic and necrotizing enterocolitis. Different types of probiotic mixtures and probiotic bacteria are utilized in the treatment of GI diseases. Probiotics have also proved its effectiveness in the treatment of gastrointestinal conditions. **Conclusion:** Efforts to improve human health are concentrating on methods for modifying the indigenous microflora using live microorganisms, now referred to as "probiotics". The probiotic market is expanding and is expected to rise to \$64.6bn by the year 2023. Probiotics are now added to a variety of food products such as cereals, fruit juices and milk-based product.

## INTRODUCTION

Probiotics are of great health benefits as they help balancing the environment and stimulating the growth of beneficial bacteria in our body [1]. Probiotics greatly enhances the bioavailability of nutrients we intake such as dietary iron, improves growth and development of human body and mind and aid in the production of B-group vitamins inside the gut [2]. They are proven effective in treating diarrheal diseases, lactose intolerance, in the prevention of diabetes, improving psychological problems and certain kinds of cancer [3]. Balanced colonization of probiotic bacteria influenced the health status of person. Probiotics are found to be an alternative of antibiotics to fight against serious disorders of digestive and nervous system [4]. There are two main categories of probiotics; dairy-based products that includes functional foods and

non-dairy-based products that are available as pharmaceutical supplements [5]. In present times, various kinds of probiotic bacteria are added to food products such as milk-based deserts, ice-cream, cheese, fermented foods, mayonnaise, cereals, fruit juices and in many other products as functional foods [6,7]. Probiotic supplements are an effective way of adding beneficial bacteria in the body and are recently emerging as an important domain of food supplements [8]. Recently, probiotics got great attention and have been enormously investigated and studied around the globe [9]. Yearly calculated global share of probiotics is approximately of worth \$15 billion USD and is flourishing year by year at an expected annual rate of 7 percent [10]. The probiotics industry is predicted to grow from \$35.6bn in 2015 to \$64.6bn by 2023 [11].

Probiotics decreased the incidence of constipation after the 12-week intervention period upto 12%, incidence of diarrhea 4.9% and prevented the occurrence of acute respiratory infection upto 15.9% in Vietnamese children [12]. Nutrition-related factors contribute to about 45% of deaths in children under-5 years of age and diarrheal diseases kills 2,195 children every day, it accounts for 1 in 9 child deaths worldwide, making diarrhea the second leading cause of death among children under the age of 5 [13,14]. The addition of probiotics to infant formula has been known to confer numerous benefits to the infant, including the improvement of gut health and immunity, countering the growth of harmful bacteria (pathogens) in the gut and enhancing overall host immune and health status. Moreover, the addition of probiotics including *Lactobacillus reuteri*, *Lactobacillus acidophilus*, *Bifidobacterium longum*, *Bacillus clausii* and *Bifidobacterium lactis* in infant formula has been shown to reduce risks associated with diarrhoea resulting from antibiotic use and the symptoms of colic [15].

#### **Mechanism of Action of Probiotics**

In a healthy body condition, non-pathogenic microorganisms provide very well ecosystem. This may be disrupted by variety of factors including diet, antibiotics and stress [19]. Formation of short chain fatty acids, expulsion of disease causing bacteria, resistance to colonization, bile site actions, enzymatic activities and immunological impacts are all included in the mechanisms of probiotic bacteria [16]. Other mechanisms include antagonism via formation of anti-microbial substances, competition with disease causing bacteria for epithelial adhesion and nutrients, modulation of the host's immune system and prevent the formation of toxic substances [17].

#### **Role of Probiotics in Gut Health**

Probiotics contain live microorganisms that can help gut microbiota to regain its normal balance and keep the gut and host healthy. Probiotic mixtures mainly contain strains of *Lactobacillus*, *Bifidobacterium*, *Clostridium* and *Streptococcus* species which upon consumption provide health benefits to the host [20]. Probiotics apply their positive impacts via regulation of microflora, maintenance of epithelial lining, maturing the immune system of body and prevention and inhibition of disease causing bacteria. Probiotics are capable of maintaining the diversity of intestinal microbiota and enhancing the immune response [21]. Probiotics also aid in maintaining the integrity of intestinal barrier, stimulate the mucosal immunity and produce metabolites that improve overall gut health [22]. Probiotics stimulate the goblet cells of the tract to secrete mucin which prevents the adhesion of disease causing bacteria [23]. Adhesion mechanism of probiotic bacteria significantly increases the chances of interaction with

host, which ultimately results in colonization of healthy bacteria and also enhances their transit time in the gut so that they can exert their positive effects [25]. In addition, probiotics also release anti-bacterial substances that cause impediment in the binding of disease causing bacteria like *H. pylori* to epithelial cells [22]. Another function of probiotics is the secretion of anti-microbial substances (organic acids) that potentially inhibits the activity of disease causing bacteria [25]. Moreover, probiotics also stimulate the immune mechanism via stimulating the formation of immunoglobulin antibodies. By this, probiotics can play their role in strengthening the immune mechanisms.

#### **Probiotics in Pediatric Gastrointestinal Diseases**

The microflora of the gastrointestinal tract varies among the individuals and also within the same individual over time. The GI tract comprises both good and bad bacteria that exist in a symbiotic relationship [22]. Variety of factors influence the microbiota of GI tract of infants including diet, antibiotics, use of gastric acid blocking substances and environment. Probiotics are proposed as a preventive measure for the treatment of wide range of childhood diseases [19].

#### **Irritable bowel syndrome (IBS)**

IBS is a functional gastrointestinal disorder that has a significant effect on the life quality and functional status of individuals. IBS is described by reoccurring abdominal discomfort that is accompanied by unusual stool form and frequency. Disrupted bowel movements in IBS include symptoms of diarrhea, constipation or the combination of two are common as well as symptoms of abdominal bloating are also present. According to studies, the prevalence of irritable bowel syndrome in children ranges between 6-14% [25]. In IBS, there is significant changes in the gut microbiota and higher proportion of Proteobacteria and genera like *Dorea*, *Haemophilus*, *Ruminococcus* and *Clostridium* as well as high ratio of Firmicutes to Bacteroidetes [23]. Probiotics have been long proposed as a way to alter the gut microbiota, regulate visceral oversensitivity and reduce the process of inflammation thus optimizing the symptoms and abdominal discomfort (pain) in irritable bowel syndrome [22]. The most researched probiotic strains in the treatment of irritable bowel syndrome are *Lactobacillus Rhamnosus GG (LGG)* and *L. reuteri DSM 17938* [24]. The probiotic strain (*L. reuteri DSM 17938*) is proven to be more efficient in easing abdominal discomfort and IBS. The utilization of probiotic strain *Lactobacillus Rhamnosus GG (LGG)* markedly reduces the severity of pain in children with IBS [26]. The probiotic mix (VSL#3) sachet contains 450 billion CFU bacteria from 8 different strains of *Lactobacillus*, *Bifidobacterium* and *Streptococcus* species. The effect of

this mixture is found to be associated with easiness of abdominal pain and bloating in infants with irritable bowel syndrome.

### **Constipation**

The prevalence of functional constipation in infants and toddlers differs among studies ranging from 5-27%. Toddlers are widely reported to have a greater prevalence of constipation as compared to infants [26]. Constipation causes symptoms like painful defecation/ bowel movements, abdominal discomfort/ pain and bowel incontinence. Probiotics have been tested as a potentially beneficial and safe treatment option for constipation. Probiotics are thought to improve muscular contractions and decrease intestinal status by altering gut flora, enhancing the formation of lactate and SCFA and decreasing luminal pH level [25]. Supplementation of probiotic species *Bifidobacterium lactis* GCL2505 and *Lactobacillus casei shirota* are found to increase the bifidobacteria in constipation. The beneficial impact of probiotics on inflammatory response thus impacts the gut motility regulation and consequently constipation [19]. In addition, different strains of *Bifidobacterium lactis* improved the gut transit time, frequency and consistency of stool and flatulence in constipation [25]. Moreover, strains of *L. casei rhamnosus* Lcr35 have been shown to facilitate the passage of hard stools [25].

### **Gastroesophageal reflux disease (GERD)**

GERD is a frequently encountered gastrointestinal disorder that mainly affects the esophagus and gastro-duodenum part. GERD is defined as bothersome symptoms that affect life quality and complications caused by the backward flow of gastric contents into esophagus and respiratory tract. GERD can cause heartburn, epigastric and retrosternal pain and the prevalence of GERD ranges from 8-33% based on age group. The path mechanisms of GERD include relaxation of esophagus sphincter muscles by retained stomach contents. It is also thought that activity of receptors in stomach mucosa which causes temporary relaxation is also included in the causes of GERD. Proton pump inhibitors are first line treatment method for GERD but prolonged use can alter the bacterial population and inhibit the gastric acid barrier resulting in dysbiosis that may lead to abdominal pain. Probiotics have been shown to improve gut health by treating the gastrointestinal functions and abdominal symptoms. Probiotics interact with receptors in gastric mucosa and speed up the passage of food through the GI tract. Probiotic strain particularly *L. reuteri* DSM17938 may improve esophageal and gastric symptoms by boosting gastric emptying [25].

### **Diarrhea**

The most severe cases of diarrhea occur in children particularly in those under the age of 5. The main agents

responsible for causing diarrhea are *E. coli* strains, *Salmonella* and *Shigella* species and in case of watery diarrhea the main agents are Rotavirus, *Cryptosporidium* and Adenovirus. Antibiotic associated diarrhea is a frequent side effect of the antibiotic therapy. Different antibiotics target the anaerobic bacteria and cause considerable disturbance in the enteric microbiome. In children, 5-40% of diarrheal cases are attributed to the use of antibiotics [24]. Probiotics have the potential to lessen the commonly occurring severe intestinal effects in antibiotic associated diarrhea. *S. boulardii* and LGG are the most impactful probiotics in children for lowering the risk of antibiotic induced diarrhea [26]. Nosocomial or hospital acquired diarrhea is a troublesome issue reported all over the world. Rotavirus is still the leading cause of severe diarrhea in young children including hospital acquired or nosocomial diarrhea. Probiotic have been studied to see if they can help prevent or lessen the severity of hospital acquired diarrhea. *Lactobacillus* has been shown to be extremely effective in the treatment of rotavirus diarrhea. The well-documented effect is a reduction in the duration of rotavirus diarrhea when *Lactobacillus* is used. In cases of *Clostridium difficile* induced diarrhea, it is found that administration of probiotics lowers the time period and frequency of diarrhea and speeds up the recovery process. *S. boulardii* CNCM I-745 is a preferred probiotic strain in the treatment of *Clostridium difficile* induced diarrhea [23].

### **Acute Gastroenteritis**

Acute gastroenteritis is characterized by the sudden occurrence of diarrhea with or without the occurrence of nausea, vomiting, temperature and abdominal pain/ discomfort. Acute gastroenteritis is still one of the most common childhood illnesses around the world. Extreme diarrheas are the leading cause of dehydration in this condition and if not treated it can lead to other health complications and death. Many guidelines advise using probiotics with proven efficacy as a treatment method in this condition. *Lactobacillus rhamnosus* (LGG) and *S. boulardii* should be considered in the management of this condition along with oral rehydration therapy. It is found that the utilization of probiotic strain (LGG) reduces the duration of diarrhea in acute gastroenteritis while the utilization of other probiotic strain *S. boulardii* lowers the risk of diarrhea.

### **Inflammatory Bowel Disease (IBD)**

Inflammatory bowel disease is a general word that encompasses of conditions affecting the intestinal mucosa including Crohn's disease and ulcerative colitis. Probiotics have been evaluated in the condition of Ulcerative colitis and found that VSL#3 is a well-studied probiotic in children. VSL#3 is efficient in stimulating and sustaining the recovery process. Another probiotic strain

known as *L. reuteri* ATCC 55730 is found to be effective in increment in the remission and also improve the symptoms associated with Ulcerative colitis. Probiotics which can significantly raise the microbial diversity are an effective treatment method for Crohn's disease. Several other studies are emphasizing the value of fecal microbial transplant as a treatment option for inflammatory bowel disease. This transplant decreases the number of pathogenic bacteria and increases the non-pathogenic strains of Bacteroids. It has been demonstrated that this transplant results in remission of disease and manage the symptoms associated with this condition [26].

### Infantile Colic

Infantile colic is described as inconsolable, inexplicable and unending crying in an apparently healthy individual which obviously leads to fatigued, disappointed and worried parents seeking to pacify their child. In infantile colic there are a high number of Proteobacteria and low levels of Bifidobacteria and Lactobacillus. Moreover, Actinobacteria and Firmicute are inversely related to the representation of infantile colic symptoms. Dysbiosis has been suggested to play a role in the pathogenesis of this condition, probiotic bacteria have been recommended as a good treatment method for this condition. It is found that *Lactobacillus reuteri* DSM 17938 at a dosage of 108 colony forming units per day considerably reduces the number of crying events in infants. The use of *Lactobacillus reuteri* is linked with a considerable decline in fecal calprotectin a level which is a clinical indicator of intestinal inflammation [25]. Oral intake of mixture of *Bifidobacterium longum* CECT7894 (KABP042) and *Pediococcus pentosaceus* CECT8330 (KABP041) considerably decreases the time and frequency of crying episodes. A probiotic preparation known as Vivomixx (oil suspension of medium chain triglycerides) containing four distinct strains of Lactobacilli, three distinct strains of Bifidobacteria and one strain from *Streptococcus* species. This multi-strain probiotic mixture reduces the minutes of crying in infants.

### Necrotizing Enterocolitis (NEC)

NEC is a serious and common gastrointestinal condition in premature infants and is the leading cause of mortality in the extremely premature infants between the ages of 2 weeks and 2 months. Probiotics are a useful intervention and act as a preventive measure for necrotizing enterocolitis due to the low ratio of *Lactobacillus* and *Bifidobacterium* in premature infants in comparison to healthy infants. Significant data support that regular probiotic supplementation in the form of liquid is sufficient to minimize the occurrence of severe necrotizing enterocolitis. It is found that supplementation of Infloran (*Lactobacillus acidophilus* and *Bifidobacterium bifidum*) in infants lowers the risk of surgical necrotizing enterocolitis.

Utilization of probiotic *Lactobacillus rhamnosus* in the form of Culturelle and Diclofor reduces the risk of NEC from 5.3 to 1.2%. Probiotic mixtures consisting of only *Lactobacillus* or in conjunction with *Bifidobacterium* lead to reduction in hospitalization or mortality [23].

## CONCLUSIONS

Efforts to improve human health are concentrating on methods for modifying the indigenous microflora using live microorganisms, now referred to as "probiotics". The preservation of normal/ healthy microflora, defense against infections, reduction of gastrointestinal conditions, and immune system activation are just a few of the health benefits attributed to probiotics. Probiotics also have a beneficial role in the treatment of gastrointestinal conditions in the infants and children. Probiotic strains that have been shown to have positive effects are utilized in the treatment and prevention of gastrointestinal conditions in the infants and children. It is concluded from the various studies that probiotics are safe to use in the gastrointestinal diseases of infant and children therefore, administration of probiotics should be strain specific and disease specific.

## Conflicts of Interest

The authors declare no conflict of interest.

## Source of Funding

The author(s) received no financial support for the research, authorship and/or publication of this article

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