



The Role of Probiotics in Children with Diarrhea or Constipation

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KEYWORDS

Probiotics, Lactobacillus, Diarrhea, Rotavirus, Constipation, Hirsprung

ABSTRACT

Probiotics are non-pathogenic living microorganisms and can encourage the growth of other microbes that can benefit the host's health when consumed in sufficient quantities. The aim of this study was to explore the role of probiotics in the management of diarrhea or constipation in children by clarifying their effectiveness, safety and mechanism of action. The type and design of this research is observational analysis with a literature review method. Data was collected from national and international journal publications via scientificdirect.com and pubmed.ncbi.nlm.nih.gov which met the inclusion criteria, namely research examining the role of giving probiotics to children suffering from diarrhea or constipation, research that has been published in the last ten years using data primary and secondary data as well as cross-sectional and cohort research designs. The dependent variable in this study is the outcome of diarrhea or constipation, and the independent variable is probiotics. Data analysis was carried out narratively. This research found that in children suffering from diarrhea, giving probiotics can shorten the duration of diarrhea, especially that caused by rotavirus. On the other hand, in children with constipation, probiotics can increase intestinal motility and shorten transit time so that stool consistency changes and the frequency of defecation increases. There is a relationship between giving probiotics to children and diarrhea or constipation.

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INTRODUCTION

Probiotics are live, non-pathogenic microorganisms and can encourage the growth of other microbes that can benefit the host's health when consumed in sufficient quantities (Andrea et al., 2018). Lactic acid bacteria (LAB), especially the genera *Lactobacillus* and *Bifidobacterium*, a normal flora in the human digestive tract, are a common source of probiotics (Zhao et al., 2022).

Acute diarrhea produces soft or liquid stools that are more than usual and last less than 14 days (Novita et al., 2023). Diarrhea occurs when the water and electrolyte mechanisms in the intestine are disturbed. Based on the pathophysiology, diarrhea can be divided into osmotic, secretory, inflammatory, and motility changes (Sari & Haryana, 2022). Most of the clinical manifestations that appear in cases of diarrhea are related to the infecting pathogen and the level of infection. Additional complications, such as dehydration and electrolyte imbalance, also depend on the nature of the infecting pathogen (Adika, 2022).

Constipation is a symptom of the disease. Three things that need to be considered when determining the presence of constipation are frequency, stool consistency, and physical examination results (Lestari, 2023). Constipation in children aged less than or equal to four years is determined by at least one of the symptoms of defecation less than three times a week, pain during defecation, rectal impaction, and feces in the stomach. (Azzahra, nd) . For children over four years old, constipation is defined as a frequency of defecation less than or equal to twice a week without using laxatives, two or more episodes of soiling or encopresis in one week, or a palpable period of feces in the abdomen or rectum during physical examination (Endyarni & Syarif, 2016).

Probiotics produce bacteriocins to stop pathogens and stimulate the production of intestinal epithelial mucin, which will prevent pathogenic germs from attaching to the gastrointestinal mucosa and improve intestinal barrier function (Palayukan, 2022). Probiotics can influence intestinal function by modulating the cytokine profile, inducing hyposensitivity, and activating local macrophages to increase antigen presentation to T cells. Then, T cells release cytokines to activate B lymphocytes, and finally, B lymphocytes synthesize IgA. Research results also show that *Lactobacillus* species can increase the production of IFN γ (gamma interferon) and IL-12, increasing the T Helper cell or Th1-type response and improving the Th1-Th2 balance. Based on these pathophysiological mechanisms, researchers are interested in discovering the role of probiotics in children with diarrhea or constipation (Mujahid, 2022).

Previous research shows that probiotics can provide positive benefits in treating constipation in children (Huang & Hu, 2017). A systematic review and meta-analysis of six randomized controlled trials showed that probiotic consumption significantly increased the treatment success rate and reduced the recurrence rate of constipation in children. Nevertheless, no significant association was detected between probiotic consumption and frequency of abdominal pain, stool consistency, frequency of pain during defecation, or frequency of fecal incontinence in children with constipation.

Other research shows that a probiotic mixture has a positive effect on constipation symptoms in children (Sadeghzadeh et al., 2014). A pilot study showed that this probiotic blend increased the frequency of bowel movements per week and stool consistency, while reducing the number of episodes of fecal incontinence per week and abdominal pain. The study recommends the need for a larger randomized placebo trial to confirm the findings.

In a general context, probiotics have been shown to be beneficial in treating a variety of digestive disorders, including acute community-acquired diarrhea, irritable bowel syndrome, and constipation. Probiotics are considered "good bacteria" that help maintain a healthy body.

The aim of this study was to explore the role of probiotics in the management of diarrhea or constipation in children by clarifying their effectiveness, safety and mechanism of action. Additionally, aims may also include providing further evidence that may assist in the development of clinical guidelines or recommendations for the use of probiotics in daily clinical practice.

METHOD

This research uses an observational analytical design with a literature review method based on several studies. Data was collected from national and international journal publications via scientificdirect.com and pubmed.ncbi.nlm.nih.gov, which met the inclusion criteria, namely studies examining the role of giving probiotics to children with diarrhea or constipation, research that has been published in the last ten years using data primary and secondary data as well as cross-sectional and cohort research designs. The dependent variable in this study is the outcome of diarrhea or constipation, and the independent variable is probiotics. Data analysis was carried out narratively.

RESULTS AND DISCUSSION

Probiotics

Microorganisms that are live and non-pathogenic and can encourage the growth of other microbes, known as probiotics, can benefit the host's health when consumed in sufficient quantities (Andrea et al., 2018). Probiotics were first used in 1965 by Lilley and Stillwell. Lactic acid bacteria (LAB), especially the genera *Lactobacillus* and *Bifidobacterium*, a normal flora in the human digestive tract, are a common source of probiotics (Zhao et al., 2022). One of the characteristics of probiotics is that they are safe for consumption and are not pathogenic, can reproduce and colonize the digestive tract, are resistant to gastric juices and bile and pass through the digestive tract, can attach to human intestinal epithelial cells, and can produce antimicrobial substances that are good for health. (Fandi et al., 2019). Probiotics produce bacteriocins and several compounds that the body needs, such as lactic acid, acetic acid, hydrogen peroxide, lactoperoxidase, lipopolysaccharide, pantothenic acid, pyridoxine, niacin, folic acid, cobalamin, biotin, and vitamin K (Zhao et al., 2022). Probiotics can be found in processed foods, such as fermented foods or drinks, or health supplements (Nurita et al., 2023).

Diarrhea

Acute diarrhea produces soft or liquid stools that are more than usual and last less than 14 days (Novita et al., 2023). Diarrhea occurs when the water and electrolyte mechanisms in the intestine are disturbed. Based on the pathophysiology, diarrhea can be divided into osmotic, secretory, inflammatory, and motility changes (Aslikhah, 2023). Malabsorption, use of drugs such as magnesium sulfate and magnesium hydroxide, malabsorption of glucose and galactose, and impaired absorption of the intestinal mucosa cause osmotic diarrhea. FollowinUnabsorbedces draw water from the plasma into the intestinal lumen. However, following a concentration gradient, secretion is directly increased or, more commonly, absorption is decreased in secretory diarrhea. Profuse diarrhea is a clinical sign of this diarrhea. In addition, this type of diarrhea will persist during fasting from eating and drinking. Enterotoxins in *Vibrio cholerae* or *Escherichia coli* infections, hormone-producing disease (VIPoma), ileal resection (impaired bile salt absorption), the effects of the laxative drug dioctyl sodium sulfosuccinate, and others are common causes of secretory diarrhea. When the intestinal wall is injured, the intestinal mucosa is damaged. This causes excessive mucus production, exudation of water and electrolytes into the lumen, and disturbances in water-electrolyte absorption, leading to inflammatory diarrhea. Visible infections, such as *Shigella* dysentery, or uninfected infections, such as ulcerative colitis and Crohn's disease, can cause inflammation of the small intestinal mucosa. Diarrhea can also occur due to diabetes mellitus, hyperthyroidism, or intestinal motility disorders after vagotomy. In addition, physiological conditions such as anxiety, drugs, and toxins can directly affect the enteric nervous system (ENS), which in turn causes intestinal motility disorders (Hartatik & Siskaningrum, 2018). This diarrhea can be caused by exposure of luminal contents to intestinal absorption surfaces, increased intestinal motility, and decreased transit time. One or more of these pathophysiologies can cause diarrhea (Oktafiani, 2020). In Table 1, you can see the difference between acute inflammatory and non-inflammatory diarrhea.

Table 1 Pathophysiology and types of acute diarrhea

	Inflammatory	Non-inflammatory
Mechanism	Mucosal invasion or cyto-toxin mediated inflamma- tory response	Enterotoxin or reduced absorption capacity of the small intestine
Location	Colon, distal small intestine	Small intestine proximal part

	Inflammatory	Non-inflammatory
Diagnosis of Causes	There are fecal leukocytes, high fecal lactoferrin levels	There are no fecal leukocytes. lactoferrin levels of low feces
Bacteria	Campylobacter* Shigella species Clostridium difficile Yersinia Vibrio parahaemolyticus Enteroinvasive E.coli Plesiomonas shigelloides	Salmonella* Escherichia coli** Clostridium perfringens Staphylococcus aureus Aeromonas hydrophilia Bacillus cereus Vibrio cholerae
Virus	Cytomegalovirus* Adenovirus Herpes simplex virus	Rotavirus Norwalk
Parasite	Entamoeba histolytica	Cryptosporidium* Microsporidium Isospora Cyclospora Giardia lamblia

Disturbances in the process of secretion of fluids and enzymes as well as absorption of nutrients in the small intestine caused by infection will cause watery diarrhea in large volumes, accompanied by stomach cramps, bloating, lots of gas, weight loss, fever is rare, in addition, the stool does not contain occult blood or inflammatory cells. Meanwhile, suppose there is a disturbance in the storage area (large intestine). In that case, diarrhea will occur more frequently but regularly and with a smaller volume and is often accompanied by abdominal pain due to bowel movements, fever, and bloody or mucoid stools are ubiquitous so that Stool examination will show positive results for inflammatory cells and erythrocytes (Anggriani et al., 2023).

Specific pathogens can cause acute diarrhea. Rotavirus and EEscherichiacoli are the most common intestinal pathogens that cause diarrhea. Rotavirus group A and serotypes G1, G2, G3, G4, and G9 cause most intestinal infections in children aged 6 to 24 months, with mild clinical symptoms, but can cause severe dehydration and even death (Rohmah et al., 2023). Enteroaggregative E. coli (EaggEC), Enterotoxigenic E. coli (ETEC), and Enteropathogenic E. coli (EPEC) types are the ones that most often cause diarrhea in children under two years old and cause long-lasting diarrhea (Rosalina et al., 2021). The most common causes of acute diarrhea with blood are Campylobacter spp, Salmonella spp, Shigella spp, and Yersinia spp. Additionally, Vibrio cholerae can also cause diarrhea, especially in areas that do not have good sanitation (Said et al., 2022). Due to food sensitivity, Enteropathy also often causes acute diarrhea due to the presence of antigens in foods that usually cause an allergic response, such as cow's milk, soya, and egg protein. Diarrheal Enteropathy has symptoms of diarrhea accompanied by vomiting due to malabsorption and failure to grow (Sukmawati et al., 2016).

Most of the clinical manifestations that appear in cases of diarrhea are related to the infecting pathogen and the level of infection. Additional complications, such as dehydration and electrolyte imbalance, also depend on the nature of the infecting pathogen. Absorption of the toxin before it forms is usually associated with rapid nausea and vomiting within 6 hours, with possible fever and abdominal cramps after an incubation period of 8–16 hours. The production of enterotoxins is associated with the absorption of these toxins. Clostridium perfringens and Bacillus cereus have symptoms of stomach cramps and watery diarrhea after an incubation period of 16-48 hours, which is associated with the production of enterotoxins, while the bacterial toxin of Staphylococcus aureus or Bacillus cereus can cause symptoms in less than 6 hours, and in viral infections it can cause

symptoms lasting longer than 16 to 72 hours, especially vomiting. Or bacterial contamination of food by enterotoxigenic/enterohemorrhagic *E. coli*.

When taking a history of patients with acute diarrhea, it is necessary to ask about the onset, duration of symptoms, frequency, and quantity and characteristics of feces (Permatasari et al., 2022). Diagnosis can also be based on the history of food consumed, as explained in Table 2. Specific pathogens are associated with consuming unpasteurized food products, raw or undercooked meat, fish, or vegetables. In addition, it is essential to thoroughly check the history of previous illnesses, including recent antibiotics (which suggest the presence of *C. difficile* infection), use of other medications, and recent antibiotics (which suggest the presence of *C. difficile* infection).

No appetite at the beginning of diarrhea, the stool has a liquid consistency and may contain mucus and blood; as time goes by, the color changes to greenish because bile mixes with it. Much of the lactic acid comes from lactose that cannot absorb diarrhea in the intestines, causing frequent defecation and more acidic stools. Before or after diarrhea, vomiting can occur and can be caused by stomach inflammation or disturbances in acid-base and electrolyte balance. General condition, consciousness, body weight, temperature, respiratory rate, pulse, blood pressure, skin turgor, eyelids, and tongue mucosa must all be evaluated during the physical examination (Mujasyaroh, 2019). Suppose a person has lost a lot of fluids and electrolytes. In that case, symptoms of dehydration begin to appear, such as a decrease in weight and skin turgor, the eyes and crown become sunken, the mucous membranes of the lips and mouth and the skin appear dry, the pulse increases but is weak, and the skin becomes dry. Cold and damp. The amount of fluid lost can be divided into mild, moderate, severe, and severe dehydration, while based on plasma tonicity, it can be divided into hypotonic, isotonic, and hypertonic dehydration. Additionally, signs of peritonitis should be looked for as they may indicate infection by invasive enteric pathogens.

Table 2 Sources of transmission of specific intestinal pathogens

Pathogens	Sources of Transmission / Risk Factors
Bacteria	
Staphylococcus aureus	Meat (beef, pork, poultry), eggs
Clostridium perfringens	Meat (beef, pork, poultry), eggs, home-cooked food products
Bacillus cereus	Meat (beef, pork), fried rice, vegetables
EHEC	Undercooked meat (beef, pork), ready-to-eat foods (half-cooked ham-burgers), salads, milk, cheese, bean sprouts/bamboo shoots, raw grains, can cause foodborne outbreaks. The elderly are more vulnerable
EIEC	Milk, cheese
ETEC	Travel to developing countries
Salmonella	Beef, pork, poultry, eggs, salads, raw milk, ice cream, vegetables, unpasteurized orange juice, ducklings, monitor lizards, venomous snake meat, cakes, seafood, shellfish, can cause foodborne outbreaks

Pathogens	Sources of Transmission / Risk Factors
Campylobacter	Poultry (undercooked, baked), raw milk, eggs, cheese, cakes
Shigella	Person-to-person transmission (for example, in day care centers), vegetables
Yersinia	Pigs, cows, milk, cheese, hemochromatosis patients, can cause foodborne outbreaks

Virus

<i>Rotavirus</i>	Penularan dari orang ke orang (misalnya, pada pusat perawatan harian, kamar anak-anak)
<i>Norwalk-like viruses (norovirus)</i>	Sekolah, asrama perawat, kapal pesiar, perkemahan, sayur-mayur, air, kerang-kerangan, makanan laut, dapat menimbulkan <i>winter outbreak</i> serta kejadian diare atau muntah dalam keluarga. Penularan lewat makanan
<i>Hepatitis A</i>	Lingkungan kumuh, kurang air bersih, pasien dan pegawai institusi, pusat perawatan harian, pria homoseksual, pengguna obat IV, wisatawan, barak militer, kerang-kerangan
<i>Adenovirus</i>	Diare pada bayi, AIDS (?)
<i>Cytomegalovirus</i>	Pria homoseksual yang terinfeksi HIV dengan AIDS, transplantasi organ

Protozoa

<i>Giardia lamblia</i>	Pusat perawatan harian, kolam renang, pelancong, salad, kue, defisiensi Ig A, dapat menimbulkan <i>waterborne outbreak</i>
<i>Entamoeba histolytica</i>	Berwisata ke daerah endemik selama >1 bulan, aktivitas seksual pria homoseksual, institusi, perjalanan ke daerah tropis, baru emigrasi dari wilayah tertentu
<i>Cryptosporidium</i>	Pusat perawatan harian, kolam renang, binatang sawah, kontaminasi suplai air di perkotaan, kue, wisatawan, pejamu <i>immunocompromise</i> , dapat menimbulkan <i>waterborne outbreak</i>
<i>Cyclospora</i>	Buah frambus (<i>raspberries</i>), wisatawan, dapat menimbulkan <i>foodborne outbreak</i>
<i>Isospora</i>	Infeksi HIV
<i>Microsporidium</i>	AIDS, wisatawan (?), air bersih (?)

Several supporting examinations are needed to find the cause of acute diarrhea: examination of fecal leukocytes and occult blood, fecal lactoferrin examination, lower gastrointestinal endoscopy, fecal culture, and examination for worm eggs and parasites. Several studies have evaluated the accuracy of fecal leukocyte examination alone or in combination with occult blood examination (Catur & Rahmatika, 2018). The ability of these tests to predict the presence of inflammatory diarrhea varies widely, with sensitivity and specificity ranging from 20–90%. Fecal leukocytes are also not an accurate predictor of response to antibiotic therapy. However, the presence of occult blood and leukocytes in feces supports the diagnosis of diarrhea due to bacterial infection, the history of the disease, and other diagnostic examinations (Wasiah et al., 2017). In general, examination of inflammatory cells in feces is necessary in patients with severe disease, which is characterized by one or more symptoms of massive (profuse) watery diarrhea accompanied by dehydration, there are many small fecal lumps containing blood and mucus, body temperature ≥ 38.5 °C (101.3°F), passing ≥ 6 unformed stools in 24 hours or illness duration >48 hours, severe abdominal pain, diarrhea in immunocompromised patients. As stated above, the limitations of fecal leuk and oocyte examination underlie the fecal lactoferrin latex agglutination assay (LFLA) development. Lactoferrin is a marker

for the presence of leukocytes in feces, but its measurement is more accurate and less susceptible to variations in specimen processing. In one study, fecal lactoferrin was present in 93% of 28 samples positive for Salmonella, Shigella, or Campylobacter and was absent in 83% of 18 samples with rotavirus or no detectable pathogen. Endoscopy is generally not needed to diagnose acute diarrhea. However, this examination can differentiate inflammatory bowel disease from diarrhea due to infection, diagnose opportunistic infections (such as cytomegalovirus) in immunocompromised patients, and diagnose ischemia in patients with suspected colitis, but the diagnosis is not yet available. Clear after clinical and radiological examination and diagnosed *C. difficile* infection and found pseudomembranes in toxic patients while waiting for the results of tissue culture examination. However, enzyme-linked immunosorbent assays (ELISA) examination of feces for toxin A have shortened the time to diagnose *C. difficile* infection and reduced the need for endoscopic examination in such cases. Although it is pretty challenging to predict the etiology of acute diarrhea due to bacterial infection based only on the clinical picture, documentation of the causative pathogen is not always necessary because most acute diarrhea due to infection is caused by viruses that are self-limited and will improve by almost half within time 3 days. Stool cultures are of little value in patients who develop diarrhea after >72 hours of hospitalization because the cause is almost always *C. difficile* infection or a non-infectious cause. Stool culture is also needed in immunocompromised patients, for example, patients with HIV, patients with co-morbidities that increase the risk of complications, and patients with underlying inflammatory bowel disease. It is essential to distinguish between recurrence and secondary infection in specific jobs, such as food handling. Sometimes, they can only return to work after the negative stool culture results. Clinicians should specify the suspected pathogen when sending stool to facilitate processing in the microbiology laboratory and determine the appropriate media, method, or stain to isolate or identify the organism of interest. Unlike worm eggs and parasites, often found intermittently, these pathogens are generally excreted continuously. Thus, a negative culture result is usually not a false negative result, and repeat specimens are rarely necessary. Other organisms that need to be considered in certain circumstances are Enterohemorrhagic *E. coli*, viruses, *Vibrio*, *Giardia*, *Cryptosporidium*, and *Cyclospora*. Examination for worm eggs and parasites only indicated persistent diarrhea (*Giardia*, *Cryptosporidium*, and *E. histolytica*), diarrhea after travel from Russia, Nepal, or mountainous areas (*Giardia*, *Cryptosporidium*, and *Cyclospora*), diarrhea in AIDS patients (*Giardia* and *E. histolytica*, other parasites), in community outbreaks of water-borne diseases (*Giardia* and *Cryptosporidium*), bloody diarrhea with few or no leukocytes in the feces (intestinal amoebiasis). Due to the intermittent excretion of worm eggs and parasites, 3 specimens are required, each taken on different days for 3 consecutive days or taking each specimen ≤ 24 hours apart.

Constipation

Constipation is a symptom of the disease. Three things that need to be considered when determining the presence of constipation are frequency, stool consistency, and the results of the physical examination. Constipation in children aged less than or equal to four years is determined by at least one of the symptoms of defecation less than three times a week, pain during defecation, rectal impaction, and stool masses in the stomach. For children over four years old, constipation is defined as a frequency of defecation less than or equal to twice a week without the use of laxatives, two or more episodes of soiling or encopresis in one week, or a palpable period of feces in the abdomen or rectum during physical examination. Pain in the rectum, inability of the anal sphincter, or excessive stools leading to incontinence can cause soiling in constipation. The child's inability to control stool output, which is often confused with diarrhea, causes the soiling that often occurs with flatus.

However, voluntary or involuntary discharge of feces from underwear is called encopresis. These complaints can appear without organic abnormalities (Endyarni & Syarif, 2016).

Three essential things that need to be known during anamnesis to identify constipation in children are defecation patterns, such as frequency of defecation, stool size, stool consistency, and pain during defecation, the general condition of the child, and a history of constipation, such as when meconium first appeared, when doing expected training. During the physical examination, the condition of the abdomen, anal sphincter tone, location, and consistency of stool in the ampulla of the rectum can be demonstrated. Fecal masses in the abdomen can be seen in the lower left quadrant, and severe constipation can be seen under the xiphoid process. Every child who experiences constipation must undergo a digital rectal examination because it can show the presence of anal fissures, pain in the anus, the presence of stool and the consistency of stool in the rectum, the presence of blood in the stool, tone, and contraction of the anal sphincter (Manoppo, 2022).

Table 3 Symptoms and clinical signs of constipation

Symptoms and clinical signs	Percentage (%)
Anamnesis	
Defecation is rare	80-100
Hard stools	58-100
Pain during defecation	50-90
Flehy stool	35-96
Fecalist incontinence	45-75
Psychological problems	20-65
Abdominal pain	10-64
Anorexia/ lack of appetite	10-47
Family history of constipation	9-49
Kelainan traktus urinarius	5-43
Abdominal distention	0-61
Vomit	8-10
Physical examination	

The presence of constipation can be identified through several supporting examinations. Plain abdominal radiographs are the most basic examination that can be used to determine the presence of sciatica or spinal abnormalities. Chronic constipation that is unresponsive to therapy can be evaluated by examining colonic transit time. Barium enemas can reveal the ganglion area, a transition area between the narrow distal area and the dilated proximal part containing the ganglion. This situation usually occurs in Hirschsprung's disease. A barium enema may also reveal an overly large sigmoid colon, megacolon, or megarectum. To identify possible Hirschsprung's disease, an additional examination known as anorectal manometry is performed in children who have severe constipation. This examination helps assess the pressure of the rectum and anal sphincter, as well as rectal sensation, recto-anal reflex, and rectal compliance. Table 4 shows several differences in symptoms and signs between functional constipation and Hirschsprung's. The Rome criteria (table 5) are more

straightforward standards established by gastroenterologists in Europe and the United States to determine the presence of functional constipation.

Some organic disorders that are often reported as causes of constipation in children include neurological disorders (multiple sclerosis, spinal cord injury, muscular dystrophy, neuropathy), endocrine (hypothyroidism, diabetes), and psychological (depreciation, autism). In addition, structural abnormalities, obstruction, and disorders of the colon and pelvic floor must also be considered.

Table 4 Differences in symptoms and signs of functional constipation and Hirschsprung's disease

Variable	Functional (acquired)	P. Hirschsprung
Anamnesis		
Onset of constipation	After the age of 2 years	From birth
Encopresis/soiling	Often	Very rare
Failure to thrive	Infrequently	Maybe
Enterocolitis	Not	Maybe
Forced exercise	Usual	Not
Abdominal pain	Sometimes	Often
Stool size	Big	Usual
Defecation-resisting behavior	Often	Infrequently
Physical examination		
Abdominal distention	Infrequently	Often
Weight gain is difficult	Infrequently	Often
Anal tone	Usual	Usual
Rectal examination	Stool in the ampulla	Empty ampulla
Malnutrition	Not	Maybe
Stool period in the abdomen	Often	Infrequently
Laboratory		
Barium enema	Large amount of feces	Transition zone
	No transition zone	Late evacuation (24 hours)
Anorectal manometry	Rectal distention caused relaxation of the internal sphincter	No fincter relaxation or paradoxical increase in pressure
Biopsy of the rectum	Usual	No ganglion cells Increased acetylcholinesterase

Table 5 Rome II criteria for determining the presence of functional constipation

Keluhan selama 12 minggu, tidak perlu berurutan, dan telah berlangsung selama 12 bulan dengan memenuhi 2 atau lebih kriteria sebagai berikut.

- *Straining* pada >1 kali dalam 4 kali defekasi
- Konsistensi tinja keras pada >1 kali dalam 4 kali defekasi
- Rasa pengeluaran tinja yang tidak komplit > 1 kali dalam 4 kali b.a.b
- Rasa adanya obstruksi atau blokade anorektal pada > 1 kali dalam 4 b.a.b
- Diperlukan tindakan manual > 1 dalam 4 b.a.b (misalnya, menggunakan jari, menyokong rongga pelvis.)
- Frekuensi b.a.b kurang dari 3 kali /minggu
- Tidak disertai tinja cair dan tidak memenuhi kriteria *irritable bowel syndrome*

DISCUSSION

The Role of Probiotics in Diarrhea and Constipation

Probiotics are a group of bacteria that produce lactic acid from carbohydrates and lower the pH of the digestive tract environment. Probiotic bacteria can thrive in an acidic environment, but pathogenic bacteria cannot live in an acidic environment. In addition, probiotics produce bacteriocins to stop pathogens and stimulate the production of intestinal epithelial mucins or MUC2 and MUC3. This increase in mucin production will prevent pathogenic germs from attaching to the gastrointestinal mucosa and improve intestinal barrier function, also known as the intestinal defense function. For experimental animals, trials of four types of probiotics produced exciting results. Probiotics can modulate the cytokine profile, induce hyposensitivity, and activate local macrophages to increase antigen presentation to T cells. T cells release cytokines to activate B lymphocytes, and finally, B lymphocytes synthesize IgA. *L.acidophilus* increased lymphocyte proliferation by 43%, whereas *L. casei* (Yakult), *L. gasseri*, and *L. thombosis* inhibited basal proliferation (14–51%), and mitogens were promoted by concanavalin A (43–68%) and LPS (23–63%). Research results also show that *Lactobacillus* species can increase the production of IFN γ (gamma interferon) and IL-12, increasing the T Helper cell or Th1-type response and improving the Th1-Th2 balance. Another study showed that the probiotic *L. rhamnosus* GG can reduce food allergies and atopic eczema. In atopic cases in children, there is a "downregulating inflammation" effect associated with hypersensitivity reactions and an "upregulating anti-inflammatory cytokines" effect, such as interleukins, IL-4, and IL-10. The studies described above show that LAB strains have different immune effects and cannot be extrapolated from one strain to another, even though each strain is closely related (Negara, n.d.).

Giving probiotics to babies aged 1-12 months can reduce the duration of acute diarrhea compared to giving them without probiotics. Another study also found that giving probiotics to children aged 6 to 24 months can reduce the length of hospital stay. Probiotic bacteria can help the process of nutrient absorption and prevent disturbances in water absorption so that feces become denser. This occurs due to the exact mechanism of zinc, namely reducing the water content in the intestinal lumen, which increases or increases the absorption of water and electrolytes. Improving stool consistency can reduce the frequency of defecation, so in this case, it is in line with Manopo's research, which found that consuming probiotics and zinc during acute diarrhea can reduce stool output (Amaliah et al., 2021).

In a study by Shornikova et al. in children with acute diarrhea aged 6-36 months who were given *L.reuteri* for 5 days, the duration of diarrhea decreased by 40 hours compared to controls of 69 hours (29-hour decrease), and the *L.acidophilus*-LGG group had the shortest diarrhea (14.4 hours). Rotavirus infection was 75% of the causes of diarrhea in Shornikova's study. Apart from increasing IL-2 and TNF-A levels, *L. reuteri* produces antimicrobial activities such as lactic acid, acetic acid, and

reuterin. Therefore, *L. reuteri* reduces urease levels in feces, preventing the development of bacteria and preventing the spread of pathogenic germs in the digestive tract. With the combination of probiotics and *L. acidophilus*-LGG, diarrhea was reduced by 38.6 hours. Guandalini et al.'s study showed that in diarrheal children aged 1-36 months, administration of a single preparation reduced the infection duration controls (58 and 72 hours). In research conducted by researchers, children aged between 6 months and 12 years given live *L. acidophilus* showed a less significant reduction than controls (54.4 and 55.1 hours). In research conducted by (Padayachee, 2016), the combination of *L. acidophilus*-*B. infantis* reduced the duration of diarrhea compared to controls (3.1 and 3.6 days), while research conducted by (Un-Nisa et al., 2022) showed that the combination of *L. acidophilus*-*B. bifidum* reduced the duration of diarrhea compared to controls (3.4 and 4.5 days). Probiotics affect the immune system nonspecifically and specifically by producing organic acids, H₂O₂, bacteriocins, increasing phagocytosis, and NK cell activity, as well as the cytokines IL2, IL-6, TNF-, IFN-, and sIgA when probiotics were coadministered with three different (*L. acidophilus*, *L. acidophilus*, *B. longum*, *S. faecium*) preparations. *S. faecium* lasted longer and more frequently compared to that. In research conducted by (Mbaye et al., 2019) in children aged 1-12 months, probiotics with the same combination of strains reduced the duration of diarrhea less than controls (49.03 and 73.03 hours, respectively). Study results may differ due to different study characteristics, and the impact of exclusive breastfeeding may influence the duration of diarrhea. This is also different from research conducted by (Costantino et al., 2021), where the bacteria *L. bulgaricus*-*L. acidophilus*-*B. bifidum*-*S. thermophilus* combined, which found that the duration of diarrhea was longer than controls were 70 and 115.5 hours. A different type of subject is outpatients who are over 12 months old and did not receive antibiotics before therapy (Wald-Dickler & Spellberg, 2019). There are few studies conducted on single *S. faecium* or *B. longum* preparations or combination *S. faecium* preparations in acute diarrhea in children. (Patel & DuPont, 2015) found that the duration of *S. faecium* diarrhea was not different from controls (115 and 115.5 hours). In adults who experience diarrhea caused by enterotoxigenic *E. coli* and *V. cholerae*, administration of *S. faecium* does not reduce the duration of diarrhea. This may be because *B. longum* and *S. faecium* do not affect phagocytic activity, and neither affects specific immunity. While *S. faecium* does not affect the immune system specifically, the probiotic *B. longum* increases IgA levels (Kadir, 2016).

Probiotics work well on certain strains of pediatric acute diarrhea. If a particular strain cures acute diarrhea, a combination with another strain of the same species or another strain of a different genus will remain effective if it does not cause an antagonistic effect. Not much only a little has been done comparing individual strains, and little is known about how well they modulate the immune system. Additionally, not much is known about how they compete with pathogenic germs. Only LGG and *L. reuteri* as single preparations in previous research was proven to reduce the duration of diarrhea, especially that caused by rotavirus (Amilah, 2023).

In constipation, bacteria that produce lactic acid (probiotics) will increase intestinal motility and reduce transit time so that stool consistency changes and the frequency of defecation also increases. An open trial showed how *Bifidobacterium breve* increased bowel movement frequency in children with functional constipation. *B. breve* also helps change stool consistency, fecal incontinence, and abdominal pain. In another open trial, a combination of probiotics *B. bifidum*, *B. infantis*, *B. longum*, *L. casei*, *L. plantarum*, and *L. rhamnosus* improved constipation symptoms. *L. casei rhamnosus* Lcr35 has also been shown to help treat chronic constipation in children. Compared with the placebo group, patients receiving Lcr35 showed softer stools and a higher frequency of bowel movements. *Reuteria* also helps the peristalsis of babies who experience chronic constipation but does not change stool consistency. Yogurt with *B. longum* increases the frequency of bowel

movements, while *B. lactis* is not practical in children with constipation. Although giving formula milk containing *B. lactis* strain DN-173010 can increase the frequency of defecation in children who experience constipation, this increase is not significantly different from the control group. Therefore, probiotics are still a study product in managing constipation in children.

There is very little data on the effectiveness of using probiotics to treat IBS in children. *Lactobacillus* had little effect on improving clinical symptoms compared with placebo (OR 1.17 (95% CI 0.62–2.21) in a 2009 Cochrane review. A six-week randomized trial compared *Lactobacillus GG* (LGG) with placebo in children with IBS showed that LGG did not help reduce abdominal pain any better than placebo. However, there were fewer cases of abdominal distension in the LGG group than in the placebo. Another study showed that LGG significantly reduced the frequency and intensity of abdominal pain compared with baseline data. In addition, patients who had abnormal intestinal permeability examination results also significantly decreased after using LGG. LGG supplementation significantly improved treatment response in individuals with functional abdominal pain and IBS subgroups compared with placebo. A six-week, randomized crossover trial using VSL#3 and a placebo in children and adolescents with IBS showed that VSL#3 was more effective than the placebo in reducing IBS symptoms, reducing abdominal pain and bloating, and improving family assessment of impairment in daily activities. However, stool patterns did not show significant differences. A crossover test showed that the probiotic mixture *Bifidobacterium infantis* M-36, *Bifidobacterium breve* M-16V, and *Bifidobacterium longum* BB536 was associated with better quality of life and reduced abdominal pain in children suffering from irritable bowel syndrome. Babies who experience infantile colic improve more quickly if given breast milk combined with *L. reuteri*. However, there is no evidence of *L. reuteri* in formula-fed babies. However, (Eor et al., 2023) found that other probiotic strains in formula-fed babies.

In a recent meta-analysis and systematic review, it has been shown that probiotics increase stool frequency in Asian children. However, there were significant differences between the included trials. (Ruff et al., 2014), probiotics do not improve stool consistency in children. In a recent systematic review of the use of pre-, pro-, and synbiotics in the treatment of pediatric FC consisting of thirteen RCTs, the majority of included studies did not find significant results on bowel frequency, fecal incontinence, and pain during bowel movements. Treatment recommendations made by AN and NASPGHAN (North et al. of Pediatric Gastroenterology, Hepatology, and Nutrition) do not support the use of usingsics in children with constipation. These recommendations are based on the evaluation of five RCTs. Both studies showed positive results (*L. rhamnosus* Lcr35, *B. longum*, and *L. reuteri* DSM17938) and negative results.

CONCLUSION

Probiotics come from lactic acid bacteria (LAB), which are normal digestive tract flora and are beneficial for health when consumed in sufficient quantities. Probiotic bacteria can thrive in an acidic environment and produce bacteriocins to stop pathogens and stimulate the production of intestinal epithelial mucin, which will prevent pathogenic germs from attaching to the gastrointestinal mucosa and improve intestinal barrier function. In diarrhea, probiotic bacteria can help the process of nutrient absorption and prevent disturbances in water absorption so that the feces become denser. Acute diarrhea itself is defined as the production of soft or liquid stools that are more than usual and last less than 14 days. Meanwhile, in constipation, bacteria that produce lactic acid (probiotics) will increase intestinal motility and reduce transit time so that stool consistency changes and the frequency of defecation also increases. Based on the Rome criteria, constipation in children is confirmed if two complaints occur within 1 or 2 weeks.

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