



## **CLINICAL USES OF PREBIOTICS AND RULE OF PROBIOTICS INFANT FORMULA IN TREATMENT OF ACUTE DIARRHEA (PROSPECTIVE STUDY)**

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### **Abstract:**

Probiotics are defined as "live microorganisms" that are part of a healthy gut microbiota and have been shown to help treat a variety of gastrointestinal diseases in kids, including acute gastroenteritis. The purpose of this review is to assess the pathogen-specific function of Supplemental probiotic use for treating diarrhea in young children. Studies looking into the effects of probiotics and synbiotics on the outcome of acute gastroenteritis with a known etiology were identified through a search of scholarly databases. There were 32 studies found; most looked at probiotics and their effect on rotavirus gastroenteritis, whereas only a few looked at probiotics and bacterial diarrhea separately. The most studied strains, including *Lactobacillus rhamnosus* (*L. rhamnosus*), *Lactobacillus reuteri*, and *Saccharomyces boulardii*, have been shown to reduce diarrhea and hospitalization time, particularly in the presence of rotavirus infection. Equally effective, and perhaps more influential on rotavirus fecal shedding, were combined preparations comprising at least one of the aforementioned strains. It has also been suggested that rotavirus immunization status is a major determining element of the effect of probiotic use. More research is needed, and larger cohort studies are necessary, because there is a dearth of studies examining bacterial etiologies and clinical trials conducted in ambulatory care units. *methods*. The total was 300 child from 20 of september 2020 to 20 of September 2022 . prospective study . Conclusio Infants with a more developed immune system, like those at five months or older, can benefit from prebiotics in their formula, and this is something that the supports.Aim Interest in probiotics continues to rise, sparked by new findings about the importance of the gut microbiota to human health. Focusing on children, the authors intended to summarize the current state of knowledge about probiotics.

**Keywords:** microbiome modifying formula; probiotics; synbiotics; rotavirus infection; bacterial diarrhea; children

### **INTRODUCTION**

Oral supplements called probiotics are characterized as having live microorganisms, such as bacteria and yeasts, that are similar to those present in the microbiota of a typical, healthy gut [1,2]. Henry Tissier was the first to note that children with diarrhea and newborns fed formula had a lower quality stool bacterial culture compared to healthy breastfed infants and those not sick with diarrhea [3,4]. While many studies have been conducted since these original findings were published in 1907, they have either been poorly designed or have relied on insufficiently cultivated

bacteria on substrates other than human milk, both of which limited their ability to draw valid conclusions. Later studies and the ability to isolate and characterize specific bacterial cultures revealed the many health benefits of probiotics, such as the enhancement of intestinal health, the reduction of lactose intolerance symptoms, and the prevention of inflammatory bowel disease, infectious diarrhea, and allergic reactions [3,5]. Their lack of negative effects and the fact that they are helpful to the host has led to their widespread use. Maintaining a healthy balance of gut microbes is



important because it helps the intestinal mucosal defense system do its job, which in turn helps the gut mount a proper immune response after exposure to non-self antigens [7]. Probiotics have been shown to inhibit pathogen binding to endothelial receptors, improve the function of tight junctions between enterocytes, increase mucin production locally (*Lactobacillus* species), and decrease intraluminal pH through the production of lactic acid and hydrogen peroxide [8,9]. As a result, the gut mucosa is better protected from external aggression and the probiotic strains themselves produce a hostile environment for potential pathogens. The effectiveness of probiotics is strain dependent. Protease-producing probiotics like *Saccharomyces boulardii* (*S. boulardii*) help the body get rid of harmful bacteria like *Escherichia coli* (*E. coli*), *Clostridium difficile* (*C. diff*), and *Vibrio cholerae* (*V. cholerae*) [10]. Conversely, lactobacilli species produce  $\beta$ -galactosidase, an enzyme that has been shown to help reduce diarrhea and aid in lactose digestion [11]. Multiple randomized controlled trials evaluated the effectiveness of probiotics in reducing the severity and duration of diarrhea-related symptoms, and the results obtained have formed the basis of meta-analysis publications [12–14]. This is because ongoing research has provided insights into the role of probiotics in modulating mucosal immune response and combating antigen invasion. Diarrhea is one of the top causes of morbidity and mortality in children younger than 5 years old [15], hence most of these published trials have involved children. *Lactobacillus rhamnosus* GG (*L. rhamnosus* GG) and *S. boulardii* were the most commonly analyzed strains [16]. These two strains, along with *L. reuteri*, are the three major probiotics universally recommended through consensus statements for the treatment of acute gastroenteritis in children. Consistent expert agreement supports the use of *L. rhamnosus* GG and *S. boulardii* for 5-7 days as adjuvant to oral rehydration solutions in childhood acute gastroenteritis in Europe, while in the United States, recommendations for the use of probiotic preparations in infectious and antimicrobial-related diarrhea in children and adults are supported by weak to moderate evidence [16,17]. Working Group on Probiotics and Prebiotics of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) 2020 Update on the Treatment of Acute Childhood Gastroenteritis also supported the use of a combination between *L. rhamnosus* and *L. reuteri* and recommended against the simultaneous use of *L. helveticus* and *L. rhamnosus* [18]. However, only a select few probiotic strains have shown advantage over placebo in reducing symptom intensity and duration of acute gastroenteritis, and are thus suggested as adjuvant therapy. When it comes to treating and

preventing conditions like *Helicobacter pylori* gastritis [19,20], managing infantile colic, or preventing antibiotic-associated diarrhea, it appears that the beneficial probiotic effects are strain specific. However, data on the pathogen-specific advantages of probiotic strains is limited, with recent research focusing on how probiotic supplementation affects the development and severity of diarrhoeal episodes with recognized causes. In light of new literature results, this review seeks to explore the pathogen-specific role of probiotic and synbiotic supplementation in pediatric acute gastroenteritis.

#### Probiotic-supplemented formula

The overall health benefit and efficacy of adding probiotics to infant formula remains to be demonstrated in large

randomised clinical trials (RCTs). A clinical report by the American Academy of Paediatrics reviewed the currently

known health benefits of probiotic and prebiotic products, including those that are added to commercially available

infant formula and other food products for children.<sup>5</sup>

The report states that the use of probiotics has been shown to be modestly effective in RCTs in treating acute viral gastroenteritis in healthy children, and preventing antibiotic-associated diarrhoea in healthy children. There is some evidence that probiotics prevent NEC in very low birthweight infants (birthweight between 1 000-1 500 g), but more studies are needed.

The committee on nutrition of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) systematically reviewed published evidence relating to the safety and health effects of the administration of formula that was supplemented with probiotics and/or prebiotics, and compared it to that on unsupplemented

formula.<sup>12</sup> The committee concluded that there currently are no safety concerns regarding feeding probiotic- and/or prebioticsupplemented formula to healthy infants, but there are insufficient data to recommend the routine use of probioticand/ or prebiotic-supplemented formula. They acknowledge the importance of more research in this field. An effective probiotic must be nonpathogenic and nontoxic and exert a beneficial effect on the host. Moreover, it should be capable of surviving passage through the gastrointestinal tract, particularly the harsh environmental conditions in the human stomach and small intestine. Probiotic supplementation in infant formula has shown that some strains may persist in the infant gut and lower stool pH.<sup>4</sup>



## **CLINICAL USES IN CHILDREN**

### **Infantile Colic**

In a randomized non-blinded trial, published almost ten years ago, 96 formula-fed infants under 4 months of age with colic received a partially hydrolyzed whey protein formula containing FOS and GOS. They experienced a greater reduction of crying episodes after 7 and 14 days compared with those assigned to a standard formula and simethicone [18]. However, whether the effect is due to partially hydrolysed protein, the prebiotics, or both, is not clear. Pärtty, *et al* [19]. studied preterm infants randomized to receive a mixture of GOS and polydextrose (1:1), probiotics or placebo during first 2 months of life, and followed-up for 1 year. In both preand probiotic groups, significantly less frequent crying was observed compared with the placebo group (19% vs. 19% vs. 47%, respectively;  $P = 0.02$ ). On the other hand, a systematic review and meta-analysis including 12 prebiotic studies found no impact of prebiotics on the incidence of colic, regurgitation, crying, restlessness or vomiting [20]. Nonetheless, adding prebiotics to infant formula for full-term infants was reviewed. Although, further confirmatory studies are needed, no adverse effects of prebiotics were found during this review.

### **Constipation**

Majority of clinical studies concerning the effects of supplementation of infant formulas with prebiotics confirmed increase in frequency of defecation and/or softer consistency of stools, similar to that of breast-fed infants [21-31]. Current analysis of stool characteristics of infants receiving short-chain GOS (scGOS) and longchain FOS (lcFOS) in ratio 9:1 showed that effects on stool consistency were more often found to be significant than effects on stool frequency [32]. Bongers, *et al.* published the only therapeutic randomized controlled trial (RCT) using prebiotic formula for functional constipation in 2007. The consumption of a high concentration sn-2 palmitic acid, scGOS/lcFOS 8g/l and partially hydrolyzed whey protein formula resulted in a strong tendency of softer stools in constipated infants, but not in a difference in defecation frequency. In a randomized, double-blind, prospective study it was shown that prebiotics can soften stools and increase stool frequency even in toddlers. A more recent study, indicated a significant rush of motilin following prebiotic supplementation. Motilin being a peptide, produced by endocrine M cells, largely presents especially in duodenum and jejunum. Its essential role is to clean undigested food from the gut by controlling inter-digestive migrating contractions. All together suggesting an association with improved gastric emptying, better tolerance to food and improved digestion in general. Changes in defecation patterns in pediatric population due to prebiotic supplementation

mostly result in improvement of abdominal comfort and reduction of prevalence of functional constipation. Since constipation affects one third of children usually before the age of five but often persists beyond puberty, these observations are relevant for preventive or curative treatment of this very common functional disorder. Yet, to establish specific doses in avoiding diarrhea, more studies are awaited.

### **Absorption of minerals**

Acidic environment in colon increases solubility of certain minerals. Bioavailability of calcium when consuming prebiotic ingredients has been well-studied. Animal studies verified the positive correlation; efficiency in humans is nevertheless not consistent. Abrams, *et al.* found significantly enhanced calcium absorption and bone mineralization in adolescents after receiving inulin-type fructans daily for a year. On the contrary, no significant effect of prebiotics was observed on calcium absorption or other markers of bone mineralisation in infants. Recent observations show that prebiotic oligosaccharides enhance iron absorption in deficient rats. Clearly, further human trials are needed, but this seems to be encouraging information, given the prevalence of iron-deficiency in children.

### **Weight-gain**

At the Summer Meeting of the Nutrition Society in 2010, it was announced that an overview of studies investigating effects of oral SCFA on appetite regulation did not reveal a positive connection. The experts concluded that sensory characteristics are those influencing our choice of which food we eat and the quantity of it rather than a physiological effect of SCFA. In children, especially in the first months of life when milk is the basic nutrition, there are some encouraging results. For instance, Mugambi, *et al.* [20] conducted a meta-analysis that summarized positive context of prebiotics in infant formulas and increased weight gain; there was no impact on length or head circumference gain. Whether this is the result of intensified energy harvests by intestinal bacteria and/or increased absorption by enterocytes is not yet clear. It is very likely that the outcome is dose-dependent [14]. Interestingly, these results are to some extent antagonistic with the inverse correlation between fibre intake and obesity known in adults as well as in adolescents. In fact, dietary fibre reduces the risk of childhood obesity by up to 21%. Furthermore, Dasopoulou, *et al.* found that supplementation of infant formula with scGOS/lcFOS resulted in significantly lower mean cholesterol values compared with preterm neonates fed with standard formula.



### **Respiratory infections**

It would be simple, safe and economical if prebiotics would help to prevent respiratory infections

### **Eczema**

Grüber and his team performed an international double-blind placebo-controlled trial in 832 low atopy-risk

infants. They were assigned either to the formula containing 6.8 g/L GOS/FOS (9:1) plus AOS 1.2 g/L, or standard formula. Results were compared to 300 breastfed infants. At one year follow-up, the prebiotic group had almost comparable incidence of eczema to breastfed babies (5.7 vs 7.3%, vs controls 9.7%).

### **Diarrhea**

An open-label RCT published six years ago included more than 300 healthy infants, age 1-2 months.

The group receiving a GOS/FOS mix had a significantly lower number of gastrointestinal infections and antibiotic use per year. Still, when Duggan, *et al.* studied a group of 282 infants 6-12 months of age, there was no difference in diarrheal prevalence or the mean duration of diarrhea between those receiving an infant cereal enriched with oligofructose with and without prebiotics. Destruction of microbial population in GIT has the power to start the so called antibiotic-associated diarrhea. Preventive intervention by giving prebiotics

after or along with antibiotic treatment has so far not been properly evaluated. A RCT published in 2006 by Brunser, *et al.* showed no significant difference in the frequency of antibiotic-induced diarrhea between two groups, aged 1-2 years. The first group received inulin and oligofructose (total of 4.5 g/L) containing milk formula for 3 weeks after they had ended amoxicillin therapy for respiratory infection. The second group received prebiotic-free milk formula. Another trial was organized by the ESPGHAN Working Group on Pro- and Pre-biotics. In this multi-centre trial,

children with oral and/or intravenous antibiotic therapy covering common infections were treated with inulin and

FOS in age-dependent doses (max 5g/day) for as long as they were taking antimicrobial drugs. These children were below 11 years old and tolerated the mixture well; nonetheless, it had no effect regarding antibiotic-associated

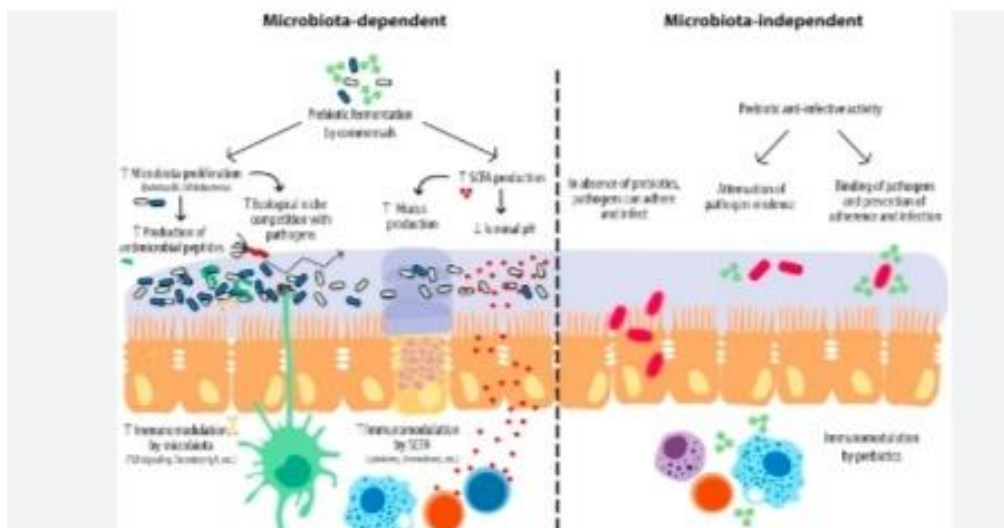
diarrhea. The study was stopped before time because of slow recruitment and the working group concluded that overall prevalence of diarrhea was not high and caution must be taken when judging the results.

However, there is a need for further research with different prebiotics. Administration of prebiotic compounds *via* oral

rehydration solution (ORS) is under investigation. A decade ago, Hoekstra, *et al.* also completed a multicentre

European double-blind randomized placebo controlled study on behalf of the ESPGHAN (European Society for Paediatric Gastroenterology, Hepatology, and Nutrition) Working Group on intestinal infection.

The subject was ORS containing a mixture of prebiotics (soy polysaccharides 25%, alpha-cellulose 9%, gum arabic 19%, FOS 18.5%, inulin 21.5%, resistant starch 7%) in the acute diarrhea treatment. Children aged 1 month to 3 years with acute diarrhea resulting in mild-to-moderate dehydration were given either supplemented or non-supplemented ORS. There was no significant difference between participants of the two groups in mean 48-h stool quantity, duration of symptoms and hospitalization. No significant influence on clinical course of acute gastroenteritis was also reported by Israeli analysts. A mixture of 80% lcFOS/scGOS and 20% AOS in a three 2-g sachets per day significantly increased stool consistency ( $P=0.048$ ) but not total of daily stools number ( $P=0.66$ ) in 9- to 24-month-old children.



**Fig.1. PREBIOTICS FOR GASTROINTESTINAL INFECTIONS**

**PATIENTS AND METHODS**

**Design of study.**..An interventional study was carried out from September 2020 to September 2022. The total numbers of cases 300 child included from both genders, their ages between 3-12 months old, prospective study.

**Statistical Analysis:**

Data entry and analysis were done using the SPSS program, version 11. Comparison of proportions was performed using chi square, P-value of less than 0.05 was considered as statistically significant, P-value <0.01

as highly significant and <0.001 as extremely significant.

**RESULT**

The total number of cases was 300 infants, were males (56%) and were females (44%) as, with male to female ratio 1.2:1. Analysis of the residency of the children aged 3-12 months revealed that (61%) from urban area and (39%) children from rural



area. Distribution of the study sample in regard to their age groups revealed that most age group affected for

both groups is 6-9 months. While 3-6 months is the least

**Table (1) effect of prebiotics on duration of diarrhea**

Cases	No. of cases	Duration of diarrhea In days (mean ±SD)	% of Total
Taken prebiotics	150	2.7(±1.7)	50%
Control	150	3.4(±1.6)	50%
Total	300	3.06(±1.7)	100%

$P$  value = 0.04 < 0.05 (significant)

**Table (2) effect of prebiotics on cure rate of diarrhea (in days) within the 1<sup>st</sup> 3 days after intervention.**

Cases	No. of cases cure within 3days		No. of cases not cure within 3days		Total	
	No	%	No	%	No	%
Taken prebiotics	102	34%	48	16%	150	50%
Control	60	19%	90	31%	150	50%
Total	162	53%	138	47%	300	100%

$\chi^2$  (chi-square) = 9.03 , df = 1 ,  $P$  value = 0.003 < 0.05 (significant)

**Table (3) effect of prebiotics on improvement of consistency of diarrhea within the 1<sup>st</sup> 3 days after intervention.**

Cases	No. of cases improve consistency within 3days		No. of cases not improve consistency within 3days		Total	
	No	%	No	%	No	%
Taken prebiotics	114	38%	36	12%	150	50%
Control	48	16%	102	34%	150	50%



<b>Total</b>	<b>162</b>	<b>54%</b>	<b>138</b>	<b>46%</b>	<b>300</b>	<b>100%</b>
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$\chi^2$  (chi-square) = 19.3 , df =1 , P value = 0.0001 < 0.05 (significant)

**Table (4) effect of prebiotics taken on improvement of fever within the 1<sup>st</sup> 3 days after intervention..**

Cases	No. of cases	Fever in day 1 (mean ±SD)	Fever in day 2 (mean ±SD)	Fever in day 3 (mean ±SD)	% of Total
Taken prebiotics	150	37.7 °C (±0.7)	37.6 °C (±0.7)	37.04°C (±0.2)	50%
Control	150	37.9 °C (±0.7)	37.3 °C (±0.7)	37.1 °C (±0.3)	50%
<b>Total</b>	<b>300</b>	<b>37.8 °C (±0.7)</b>	<b>37.4 °C (±0.6)</b>	<b>37.08°C (±0.2)</b>	<b>100%</b>
<b>P value</b>		<b>0.5 &gt;0.05 non significant</b>	<b>0.7 &gt;0.05 non significant</b>	<b>0.1 &gt;0.05 non significant</b>	

**Table (5) effect of prebiotics on improvement of stool frequency of prebiotics on improvement of fever.**

Cases	No. of cases	Frequency in day 1 (mean ±SD)	Frequency in day 2 (mean ±SD)	Frequency in day 3 (mean ±SD)	% of Total
Taken prebiotics	150	9.7(±3.7)	6.6(±4.1)	3.8(±2.2)	50%
Control	150	8.9(±2.9)	8.2(±3.2)	5.3(±2.6)	50%
<b>Total</b>	<b>300</b>	<b>9.2(±3.3)</b>	<b>7.4(±3.7)</b>	<b>4.6(±2.5)</b>	<b>100%</b>
<b>P value</b>		<b>0.1 &gt; 0.05 non significant</b>	<b>0.03 &lt; 0.05 significant</b>	<b>0.003 &lt; 0.05 significant</b>	

**Table (6) effect of prebiotics on Rota virus diarrhea .**

Cases	No. of cases cure within 3days		No. of cases not cure within 3days		Total	
	Rota V. +ve	Rota V. -ve	Rota V. +ve	Rota V. -ve	No	%
Taken prebiotics	12	90	18	30	150	50%
Control	30	30	30	60	150	50%



<b>Total</b>	<b>42</b>	<b>120</b>	<b>48</b>	<b>90</b>	<b>300</b>	<b>100%</b>
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**Table (7) effect of prebiotics on PH of stool**

<b>Cases</b>	<b>No. of cases cure within 3days</b>		<b>No. of cases not cure within 3days</b>		<b>Total</b>	
	<b>Ph of stool N.</b>	<b>Ph of stool acidic</b>	<b>Ph of stool N.</b>	<b>Ph of stool acidic</b>	<b>No</b>	<b>%</b>
<b>Taken prebiotics</b>	<b>90</b>	<b>12</b>	<b>18</b>	<b>30</b>	<b>150</b>	<b>50%</b>
<b>Control</b>	<b>54</b>	<b>6</b>	<b>66</b>	<b>24</b>	<b>150</b>	<b>50%</b>
<b>Total</b>	<b>144</b>	<b>18</b>	<b>84</b>	<b>54</b>	<b>300</b>	<b>100%</b>

**DISCUSSION**

Approximately 300 kids were a part in this. 50/50 split between experimental and control groups with prebiotics and acute diarrhoea. The target demographic consisted of male and female newborns aged three to twelve months. There are elements of both urban and rural life. Patients seen in the study's primary care centers were considered to be typical of the community at large, which would indicate that urban areas were the likely points of origin for the vast majority of cases. The ratio of men to women was 1.2 to 1, suggesting a slight preference for men. in agreement with studies by Nasheit A. Nasheit of Iraq's Al- Nahrain University. More promising results were found by Rekan Sulaiman. There are more men than women working at Karbala Hospital (66.6% to 33.2%). It also lent credence to findings made by Mona J. Ali. According to a statistical analysis of all occurrences of diarrhea, the most common age is between 6 and 9 months. Because their immune systems are still maturing, young children are more likely to contract gastroenteritis when they are initially exposed to solid foods. The findings of researchers Muna Ali and Nasheit A. Nasheit supported this conclusion. When compared to standard formula, the usage of prebiotics significantly reduced the duration of diarrhea. People who took prebiotics experienced shorter diarrhea episodes, lasting 2.7 days on average. The regular formula group returned to normal in 3.4 days. (P 0.04) There was a difference of (16.8) hours in time. Prebiotics showed promise in alleviating acute gastroenteritis in infants (3-12 months of age). No overtly unfavorable effects to prebiotics were seen. Because the use of prebiotics to treat severe diarrhoea is so cutting-edge, I have just a small sample size to use as a baseline in my own research. Annalisa Passariello

and Terrin G et al. conducted study in the field of pediatrics at the University of Naples Federico II in Naples, Italy, in 2008, and their results jived with these. Acutely ill children (aged 3 to 36 months) were split into two groups and given either the standard hypotonic ORS (group 1) or a new hypotonic ORS formulation (group 2). second-generation prebiotics. The major outcome measure was the rate at which patients' diarrhoea resolved itself within 72 hours. By the 72-hour point, more patients in Group 2 had recovered from their diarrhoea (50% vs 72.9%, P =.010). These findings support the use of prebiotics in combination with ORS for the treatment of diarrhea in children. Oral rehydration salts (ORT) and prebiotics are an effective treatment for acute diarrhoea, as shown by the research of Jessica Hersman. Both of these contrasts have significance levels below 0.001, although the gap between the two is much wider for the later (78.5 vs. 115.5 hours). My results disagreed with those of Michael de Vrese and Philippe R. Marteau. Animal experiments have shown some promising results, and prebiotics like inulin, oligofructose, and galactooligosaccharides have been shown to have beneficial effects on intestinal microflora; however, the authors of this study conclude that there is not yet enough evidence to recommend prebiotics for the treatment or prevention of diarrhoea. Only 47% of patients in a study involving 200 needed more than 3 days of treatment before they were considered healed. After three days, 72% of prebiotic users saw a reduction in diarrhoea symptoms, compared to 19% of control users. This conclusion was supported by both Annalisa Passariello A (72.9%) and Terrin et al (50.0%). Timely treatment of diarrhoea is essential for reducing the risk of dehydration, hospitalization, and malnutrition. It





saves money and helps parents avoid missing work less frequently. Loose stools are one of the hallmarks of the diarrheal illness. In this investigation, parents' accounts of their children's bowel movements were used to categorize stools as liquid, semi-liquid, or well-formed. Using data from an earlier study, we were able to compute the findings of the first three days of the experiment and find that prebiotics increase stool consistency. The results show that twice as many patients had an improvement in stool consistency compared to the controls. These results corroborated those of a study by medical doctor Jessica Hersman. She reasoned that regular bowel motions would indicate improvement. Stool consistency, as graded on a scale from 1 to 4, significantly improved the day after therapy initiation ( $p < 0.001$ ). Her findings demonstrated that prebiotic-treated subjects returned to normal bowel regularity sooner than the controls. Possible explanation: prebiotics encourage the growth of stomach bacteria that aid in the treatment of diarrhea. Throughout the entirety of our search, we did not come across any studies that challenged my results. That could be due to the fact that not many research have been done on the subject, or that the results of those that have been kept under wraps. Our findings indicate that prebiotics reduce the frequency of bowel movements rather quickly, within three days. This is when the risk of becoming dehydrated is most, according to studies. The increase in bifidobacteria seen after giving a prebiotic-fortified milk formula implies that this approach may aid in reestablishing the normal balance of gut flora. Several studies have looked into ways to reduce diarrhoea, however most of them haven't used 24-hour frequency as a criterion. Total stool production would have been a more sensitive indicator, however it was not an option for us in our study. In this instance, my results coincided with those found in the research conducted by Passariello A. and Terrin G. Both after 24 hours (4.5; 95% confidence interval 3.89-5.11 versus 5.9; 95% confidence interval  $P = .002$ ) and 48 hours (4.5; 95% confidence interval 3.89-5.11 versus 5.9; 95% confidence interval  $P = .002$ ), there was a statistically significant difference in the number of daily outputs between groups 1 (controls) and 2 (prebiotics). We found that 28% of the patients we analyzed were infected with the human rotavirus. Despite the fact that 72 of 74 samples (72%) came out negative. Dr. Ali Jerin Hasson identified a worse consequence, and this one is even worse. Possible explanations for the discrepancy include the different sample sizes used and the fact that patients in our trial were younger than two years old while those in the other study were older. Comparative studies in

Russia (34.9%), Turkey (39.5%), and Australia (40.0%) had higher response rates. While we used a latex agglutination test, other studies have used an ELISA approach, and their sample ranges have included both inpatients and outpatients, suggesting that the variation may be attributable to the technology used to detect the virus. The significant difference between the HRV detection rates of inpatients and those of outpatients is one potential explanation for the inconsistency among studies. Our data suggest that prebiotics do not contribute to rotavirus-related diarrhea. An AAP paper summarizes the present state of knowledge about the advantages of probiotics and prebiotics, especially those added to infant formula and other children's dietary products, for their health. A report by Dr. Laurie Barclay, published on December 2, 2010, corroborates these findings. He concluded that probiotics may be helpful in treating rotavirus gastroenteritis and infantile colic in babies, but that prebiotics are not. The sample size is too little to draw any judgments on whether or not prebiotics are effective in treating acute gastroenteritis. The latex method is another questionable technique with room for error when used to detect human rotavirus. [ The current understanding of prebiotics and their effect on diarrheal stool pH in extreme situations. Our study found that most patients whose stool pH was too low to be deemed normal did not show improvement within the first three days of treatment. The importance of testing stool pH in identifying cases of severe diarrhoea has been emphasized by a number of papers. These results were corroborated by research done at the Pediatrics Teaching Hospital in Erbil. Both acute and chronic diarrhoea are characterized by an intolerance to complex carbohydrate sugars (particularly lactose). Buttock excoriation is a common symptom of this illness. Breastfed and bottle-fed infants were more susceptible to the disease. Both this study and the one by Szajewska et al. found similar results. Children with a  $pH > 5.5$  in a study of 108 children aged 3 to 36 months with acute diarrhoea and dehydration had more frequent bowel movements and drank more oral rehydration therapy (ORT) in the first 24 hours. Prebiotics were not associated with any positive effects on acute diarrhea caused by a low pH. Prebiotics have the same effect on bowel movements of all kinds, independent of the stool's pH. This is in line with the findings of a previous study including adults by Levri KM. et al. They looked for controlled experiments that measured hydrogen in the breath between 1966 and 2002. Databases The reviewers came to the conclusion that prebiotic supplementation had no effect on lactose intolerance symptoms in adults. Some evidence



suggests that certain doses and formulations are effective. More trials utilizing specific strains and dosages are needed to define this potential therapeutic relationship. We infer that this result is because either there is no overarching recommendation for the use of prebiotics in the management of lactose intolerance, or the sample size was too small to draw any definitive conclusions. Fever reduction in Group 1 began earlier and was more rapid than in the controls after the first three days of treatment with prebiotics. This finding can probably be explained using the same reasoning presented there. The same logic applies to the favorable effects of using a prebiotic to increase the amounts of beneficial bifidobacteria when treating diarrhea. Our results may not be entirely trustworthy because we only collect temperatures once a day, which in cases of intermittent illness may not be during the fever's peak. Since there was no standardized antipyretic treatment or drug available, parents relied on a wide range of remedies to bring down their children's temperatures. Expenses, risks, and consequencesThe price of prebiotics and probiotics should also be taken into account. The patient must weigh the cost of a probiotic against the benefit of having fewer hours of diarrhea due to an infectious cause. However, probiotics provide a societal and economic benefit in the event of hospitalization, should the scant data suggesting a 24-hour reduction in hospitalization duration be validated.<sup>100</sup> In outpatient settings, probiotics rarely cause any adverse reactions. Low rates of systemic infection in adults (between 0.05 and 0.40%) have been found in large-scale epidemiological investigations conducted in areas where probiotic usage is endemic.<sup>101</sup> There have been reports of severely ill people developing *Saccharomyces* fungemia after receiving the probiotic through an enteral feeding tube or central venous catheter.<sup>102</sup> Careful evaluation of the risk-benefit ratio is required before probiotic administration is explored in hospitalized patients.<sup>102</sup> Probiotics should be administered in a safe manner to protect patients.<sup>102</sup> Strain specificity is crucial in the case of probiotics. Probiotics were previously only considered in the context of complementary and alternative medicine, but have recently begun to find their way into standard medical practice.<sup>103</sup> Therefore, probiotics are increasingly given to very unwell patients. Research on the effectiveness of probiotics for people with cancer is underway. Probiotic treatment and intestinal cleansing appear to have the same protective effect against infection and death in adult critically sick patients.<sup>104</sup> Predictively high-risk patients for severe acute pancreatitis who took a multispecies probiotic preparation had an increased risk of mortality

and did not experience a reduction in the risk of infectious complications.<sup>105</sup> This research shows that there are potential risks associated with probiotic use. Experimental colitis in GF IL-10<sup>-/-</sup> mice shows that the conventional probiotic *Bifidobacterium animalis* can cause severe duodenal and mild colonic inflammation and TH1/TH17 immune responses.<sup>106</sup> It's possible that this commensal bacterium species could cause illness in a susceptible host.<sup>103</sup> Multiple probiotic strains have been proven to either decrease or increase the prevalence of allergic sensitization.<sup>107</sup> High rates of gastrointestinal (GI) adverse effects and even heat-killed bacteria have been linked to the termination of trials.<sup>108</sup> Some in vitro effects may only be evident at low bacterial concentrations,<sup>92</sup> and high dosages may have the reverse impact on cultured cells.

### CONCLUSION AND RECOMMENDATIONS

Most research into the effectiveness of probiotics has focused on rotavirus infection, with multiple studies suggesting that common probiotics like *S. boulardii*, *L. reuteri*, and *L. rhamnosus*, as well as synbiotic products containing at least one of these three strains, can reduce the severity and duration of diarrhea associated with rotavirus infection and the length of time patients spend in the hospital. However, there is a lack of information on how probiotics affect diarrhea episodes treated in outpatient settings or how their use correlates with rotavirus immunization status. Although there is a lack of clinical data on the potential usefulness of probiotics in bacterial diarrhea, it has been demonstrated that specific strains can decrease the growth of certain microbial pathogens in vitro. The effects of different probiotic strains on the outcome of juvenile gastroenteritis caused by known pathogens should be evaluated in future studies using bigger cohorts. Prebiotics appear to be attractive in the prevention and treatment of many clinical disorders because, unlike probiotics, they may have a more widespread influence on the whole bacterial community in the gut, both in terms of its makeup and functionality. Encouraging additional research in the near future.

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