

Prebiotics in Dietary Management of Pediatric Gut Disease

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Abstract

Prebiotics are substrates that host bacteria preferentially use to provide health benefits. Studies on prebiotics in children are scarcer than those on probiotics. Prebiotic-supplemented infant formula has been used in the majority of research, however there have been very few reports of employing add-on prebiotic supplements to prevent or cure gastrointestinal issues in children. The aim of this study was to evaluate effect of Prebiotics in Dietary management of pediatric Gut disease. This was a cross-sectional, case-control study using interviewer-administered questionnaires to survey prebiotic use in children with Gut disease. The Maternity and Children Hospital Makkah - Makkah Health Cluster was the recruitment site for participants. After attending outpatient clinic, 30 patients with gut disease and on prebiotics were questioned, while healthy controls were those who regularly attended clinics with gut disease and not on prebiotics. The findings emphasize the predominance of male participants and younger age groups, with gastrointestinal system issues being the most frequently reported medical condition. There were varied patterns of prebiotic use and participant experiences. Regarding the forms of prebiotics used, the majority of participants (66.7%) opted for syrups or drops. Participants also reported various side effects. The most common side effect was gas (46.7%). Regarding satisfaction with prebiotic use, 63.3% of participants expressed full satisfaction. We concluded that prebiotics are now acknowledged as a promising therapeutic tool for promoting general health and preventing and treating a variety of disease states in children. Indeed, the positive clinical use of prebiotics appears promising given the incredibly low risk of severe side effects, their ease of administration, and their potent ability to affect the makeup and function of the microbiota in the gut and beyond.

Keywords: *Prebiotics, Microorganisms, Gastrointestinal Disorders, Supplementation.*

Introduction

Gibson and Roberfroid originally described the prebiotic notion in 1995 as a nondigestible dietary item that has a positive effect on the host by specifically promoting the growth and/or activity of one or a small number of bacteria that are already present in the colon. [1]

"Selectively fermented ingredients that allow specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health" was the revised definition of prebiotics in 2004. As per this description, a prebiotic needed to be resistant to host digestion, fermented by intestinal microbes, and able to specifically promote the proliferation and/or activity of beneficial intestinal bacteria. [2]

But more recently, in 2017, the International Scientific Association for Probiotics and Prebiotics changed the definition of a prebiotic supplement to "a substrate that is selectively utilized by host microorganisms conferring a health benefit" in order to reflect the most recent scientific and clinical advancements. By including substances other than carbohydrates, possible applications outside of the digestive system, and a number of non-nutritional settings, this concept expands the meaning of prebiotics. [3]

These compounds must exhibit particular characteristics that will be examined in both in vitro and in vivo studies on various subjects (e.g., humans or animals): (3) growth promotion of intestinal bacteria that are beneficial to health and well-being; (2) fermentation by intestinal microbiota, which can be assessed in vitro by adding the corresponding carbohydrates to colon content suspensions or pure or mixed bacterial cultures

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in an anaerobic batch or continuous culture fermentation system; and (3) resistance to gastric acidity, hydrolysis by digestive enzymes, and gastrointestinal absorption. [4]

Plant-derived prebiotics, including pectins, inulin, fructo-oligosaccharides (FOS), and galacto-oligosaccharides (GOS), as well as human milk oligosaccharides (HMOs), like 2'-fucosyllactose (2'-FL), and manufactured prebiotics that are added to infant formulas to mimic the functional properties of HMOs, are the most frequently researched prebiotics. [3]

Because the various prebiotic substances have different mechanisms of action, controlled clinical trials are necessary to demonstrate health benefits, just like with all other "biotics." Prebiotics have previously been linked to a number of health advantages for both adults and children, including those related to the cardiovascular, gastrointestinal, and bone metabolism systems. [3]

It was difficult to make any firm conclusions from literature about effect of Prebiotics in Dietary management of pediatric Gut disease because of the small number of samples and variability of the many studies that were evaluated in the literature.

Research Problem

The diagnosis and categorization of functional gastrointestinal diseases in children have advanced significantly, although the cause is still unknown. Despite being a functional condition that affects many early infants, infantile colic is still not well understood. Recent research has linked disruptions in the gut microbiota to colic by affecting gut motility, which in turn might affect gas production and, consequently, prolonged crying. Recent research indicates that children with colic have a less varied microbiome and lower concentrations of lactobacilli and bifidobacteria when compared to controls. [5]

There are no published randomized controlled trials that look into the impact of prebiotics on functional abdominal discomfort and irritable bowel syndrome in children. There are still many unsolved issues regarding the clinical importance, efficacy, mechanism of action, and potential long-term negative effects of these drugs, in addition to the calls for their free usage. This emphasizes the necessity of more thorough studies on the variety and therapeutic utility of prebiotics in both health and illness.

Significance of the Research

Prebiotics are now known to be a viable therapeutic strategy for improving general health as well as for the prevention and treatment of a variety of disease states in children. Prebiotics appear to have a promising future in the beneficial therapeutic application of gut microbiota composition and function, especially given their extremely low risk of major adverse effects, convenience of administration, and tremendous potential. Prebiotics are becoming more and more recognized as an immunoactive component with potential long-term benefits. This idea will develop further to include novel health potentials in the future that may be used to any microbial population to have positive benefits outside of the food and pharmaceutical industries. The creation of carefully chosen prebiotic compounds with certain functional characteristics is an appealing and feasible future accomplishment as technology develops.

Prebiotics are substrates that provide health benefits by being specifically used by the host bacteria. There are fewer studies on prebiotics in children than there are on probiotics. Prebiotic supplements added to newborn formula have been the subject of most research; nevertheless, there are very few reports of prebiotic supplements used in addition to formula to treat or prevent paediatric gastrointestinal diseases. So, the purpose of this study was to assess the role that prebiotics play in the dietary control of pediatric gut disorders.

Research Questions

- What is the effect of Prebiotics in Dietary management of pediatric Gut disease?

- Can add-on probiotic supplementation for children prevent or treat Gut disease?

Research Objectives

This study aimed to evaluate effect of Prebiotics in Dietary management of pediatric Gut disease.

Structure of the Thesis

Chapter one: Introduction

Chapter two: Review of literature

Chapter three: Methodology

Chapter four: Results

Chapter five: Discussion and Conclusion

Chapter Two: Review of Literature

Definition of Prebiotics

Over the past 20 years, the concept of prebiotics has changed considerably. "A non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health [1]" is how the term prebiotics was originally used in 1995. In early discussions, only drugs that affect a small number of gut bacteria—specifically, lactobacilli and bifidobacteria—were taken into consideration. "Selectively fermented ingredients that allow specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health" was the revised definition of prebiotic in 2004. This imposed the requirement that the claimed beneficial effects be demonstrated in the target host. Prebiotics should do this by preventing host digestion and facilitating gut microbial fermentation [2].

In 2010, the International Scientific Association for Probiotics and Prebiotics (ISAPP) released a consensus statement revising the definition of dietary prebiotic as “a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health [6]” in light of developments in molecular techniques and mounting evidence regarding the diversity and density of bacterial communities. The number of bacterial species included in this revised definition is not specified. The full length of the GI tract is now taken into consideration, rather than just the colon.

Prebiotics are "non-digestible compounds that, through their metabolization by microorganisms in the gut, modulate the composition and/or activity of the gut microbiota, thus conferring a beneficial physiological effect on the host," according to a 2015 proposal by Bindels and colleagues [7]. This modification restricted the use of prebiotics to interactions with gut microbiota, so excluding extra-intestinal habitats such the skin, respiratory tract, and vagina, even though it removed microorganism specificity and selective fermentation processes as necessary prerequisites [7]. With the most recent scientific and clinical advancements at its disposal, ISAPP met again in December 2017 to broaden the definition of prebiotic to include "a substrate that is selectively utilized by host microorganisms conferring a health benefit." As a result, prebiotics are no longer bound to the GI and are not just found in food or carbohydrates, even though they still have the health benefits associated with the microbiota. They now apply to extra-intestinal tissues and include non-food components. Moreover, animals are now included in this definition [3].

Mechanism of Action of Prebiotics

Prebiotics' mode of action is still somewhat unclear, despite numerous advancements in this area. Indirect effects are thought to play a major role in the prebiotics' mode of action. This includes serving as a source of energy for the GI tract's resident, health-promoting microbes to selectively ferment food, which is necessary for pathogen defense, intestinal barrier function, immunological system coordination, and brain function [8]. Selective fermentation produces short chain fatty acids (SCFAs) as its primary byproduct. By giving the gut epithelium a source of energy, they mediate the direct actions of the prebiotics. By increasing accessibility to transcription factors, strengthening the intestinal barrier by controlling the assembly of tight junction proteins, and promoting gut motility, metabolite absorption, sugar and lipid homeostasis, and immunological function, they also contribute to local gene expression (figure 2.1). The main SCFAs produced during fermentation are butyrate, propionate, and acetate. They help reduce the pH of the stomach to levels that prevent the growth of infections, in conjunction with lactic acid [9]. Additionally, SCFAs are believed to boost the production of mucin, which may help reduce the likelihood of bacteria crossing the intestinal barrier. By attaching themselves to the bacterial binding sites on the enterocyte surface, prebiotics like GOS can directly inhibit the growth of harmful bacteria on intestinal epithelial cells [10].

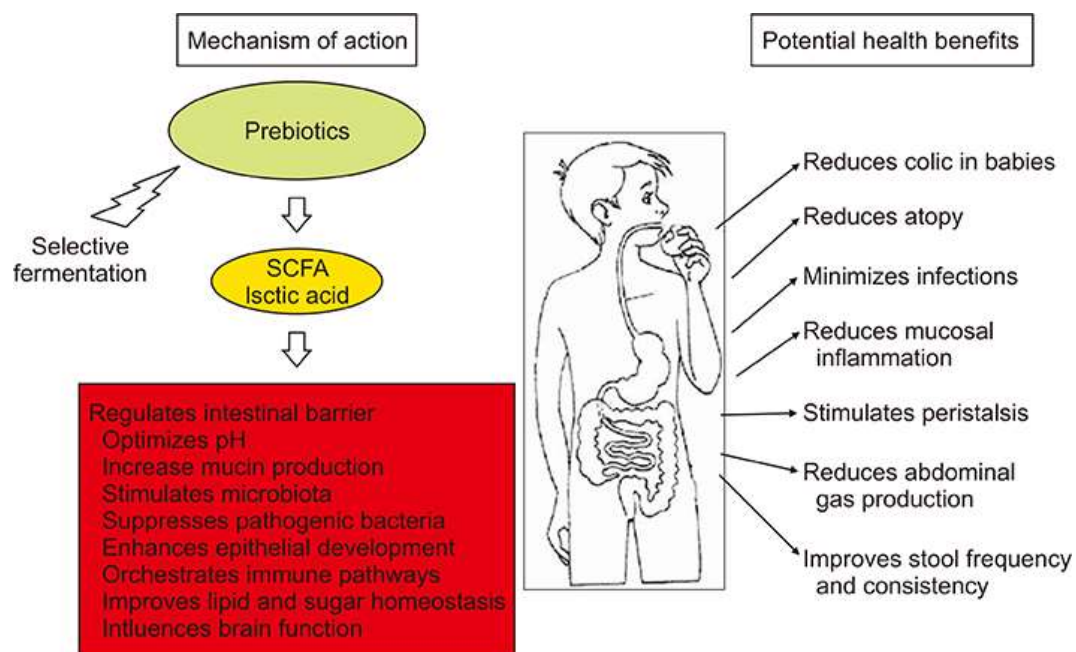


Fig. 2.1 Diagram showing the prebiotics' mode of action and possible health advantages. [11]

The Intestinal Tract and Developing Gut Microbiota

The greatest mucosal surface in the body covers the thin layer of epithelium that lines the gastrointestinal (GI) tract. In addition to absorbing nutrients, it protects the body against a variety of substances that could be harmful, poisonous, contagious, or cancerous [12]. A diverse ecology of gut microbiota coexists symbiotically with the host within the intestinal tract. While the host can simultaneously affect the gut microbiota through dietary changes, the microbiota can interact with the human body to affect how the host responds to the diet [13]. There are signs that suggest the infant's stomach may already be colonized while still in utero. The bacteria that are given to newborns will encourage colonization, which will continue until the child is three to six years old, at which point the ecosystem will stabilize [14]. In the mature adult gut, the microbiota eventually reaches 10¹⁴ microorganisms, which is equivalent to the number of eukaryotic cells in humans [15]. Among other things, the gut microbiota plays a significant role in GI health by protecting against infections, assisting with nutrition metabolism, vitamin production, and mineral bioavailability [13].

Additionally, there is mounting evidence that it may help guard against conditions like necrotizing enterocolitis, diabetes, obesity, and inflammatory bowel disease [16]. Furthermore, it is thought that there is a crucial period in the first 1000 days of life when factors affecting an infant's immune system and microbiota may have an impact on the development of disease in later life. In particular, the gut microbiota's makeup has a significant impact on immune system development, albeit direct effects that are independent of the microbiota have also been shown [17]. Short-chain fatty acids (SCFA), which are byproducts of microbial fermentation, are one important way the microbiota influences the immune response. Furthermore, SCFA are significant host modulators. For instance, butyrate provides energy to the host epithelial cells, and low butyrate levels alter the cytokine production profile of TH-cells while preserving the integrity of the intestinal epithelial barrier. Through the G-protein-coupled receptor GPR43, SCFA acetate prevents intestinal inflammation [18]. Although a healthy gut microbiota is made up of a wide variety of microorganisms, the diversity of the microbiota is lower in children under the age of three than in adults [19].

Surprisingly, children's microbiomes exhibit greater interindividual heterogeneity than adults. The facultative anaerobes, such as Enterobacteriaceae, which are thought to reduce the amount of oxygen still in the baby's stomach, start the process of gut colonization after birth. These bacteria will produce additional anaerobic conditions in a few days, which will lead to the emergence of strict anaerobes such as Clostridiaceae and Bifidobacteriaceae. However, a number of factors can significantly alter and have a considerable impact on this typical microbiota composition. [20]

First, the way a baby is delivered is thought to have a significant impact on how their gut microbiota gets colonized [21]. The type of microbiota the newborn came into contact with at birth is reflected in their gut flora. Infants born vaginally have a gut microbiota that is similar to the mother's vaginal microbiota, while infants born via Caesarean section (C-section) have a gut microbiota that is similar to the skin microbiota [22].

Second, the composition of the microbiota is affected by nursing as opposed to formula feeding. In addition to introducing novel microbial communities, breast milk includes human milk oligosaccharides (HMOs) that preferentially promote the growth of bacteria that are believed to be beneficial to health, such as Lactobacillus species and Bifidobacteria [22]. That's why infant and follow-on formula now contains prebiotics such as galactooligosaccharides, long chain fructooligosaccharides (lcfOS), and/or inulin. The presence or absence of prebiotics in the formula milk affects the microbiota of formula-fed infants, which has a more varied species that resembles an adult-like microbiota [23].

Third, the gut microbiota is altered during the weaning phase when the child is exposed to a range of solid meals. The newly accessible substrates and the cessation of breast or formula milk have a significant impact on the shift in gut microbiota makeup. The gut microbiota of infants has genes that encode enzymes capable of breaking down indigestible plant-based polysaccharides before solid foods are introduced. Thus, simple plant-based diets that include fiber and polysaccharides can be metabolized by the baby's microbiota. Long-term health across generations may be at risk if fiber and prebiotic fermenting bacteria are not passed from mother to child [24].

Lastly, other variables that can affect the microbiota's composition are discussed elsewhere. These include the use of antibiotics before and after pregnancy, preterm delivery, geographic impacts, host genetics, food, stress, and cleanliness. Modifying the gut microbiota and influencing health can be achieved by incorporating dietary fibres or prebiotics into the diet. [25]

Application of Prebiotics in Clinical Practice

A 9:1 combination of short-chain GOS (scGOS) and long-chain FOS (lcFOS), the predominant short chain to mimic the composition found in breast milk, was the most frequently studied prebiotic, according to a 2011 systematic review by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. GOS, acidic oligosaccharides (AOS), GOS/FOS/AOS, oligofructose plus inulin, and polydextrose plus GOS (with or without lactulose) were among the other

prebiotics that were investigated. In diverse investigations, the period of the intervention varied from 2 weeks to 6 months, and the doses of different prebiotics ranged from 0.15 to 0.8 g/100 mL [26]. It was challenging to make any firm conclusions based on these findings because of the small number and diversity of the different studies that the working group analyzed. Nonetheless, prebiotics' possible positive effects were acknowledged; they included enhancing gut immunity, lowering the incidence of certain atopic disorders, and reducing inflammation and recurring infections. The ESPGHAN working group also valued the use of prebiotics for functional disorders, and the Dutch group further evaluated this application in a systematic review in 2016 [26].

Prebiotics and Gut Immunity

Mature lymphocytes in the gut mucosa much exceed those in the bone marrow, and the GALT is the biggest lymphoid tissue in the body. The immune system and gut bacteria work together in concert to enable the host to withstand the high concentration of antigens in the gut. Prebiotics are believed to have their positive effects by modifying a number of GALT-associated immune processes. This is thought to be achieved indirectly by growing the numbers of good bacteria in the gut, particularly lactic acid-producing bacteria and bifidobacteria. The expression of proinflammatory cytokines is decreased by these prebiotics, while that of anti-inflammatory cytokines is increased [27]. One of the SCFAs, butyrate, was linked to a decrease in IFN- γ production and an increase in T-regulatory cells. These results imply that butyrate is a significant negative regulator of inflammation, as do its effects on colonic epithelial proliferation and barrier function. Furthermore, it has been demonstrated that acetate, the most prevalent SCFA in the colon, has anti-inflammatory properties via certain receptors found in peripheral blood cells and adipose tissue. Because of its high blood content, it is thought that other autoimmune illnesses may also exhibit systemic anti-inflammatory effects of this SCFA [28].

It is generally known that intestine secretory IgA levels and Bifidobacterium levels are correlated. Intestinal secretory IgA concentration at weeks 8 and 26 did not differ from the control group when a particular mixture of 0.6 g/100 mL of a GOS and FOS in a 9:1 ratio was added to infant formula; however, after 26 weeks of the intervention, a significant difference was observed that was comparable to the breast-fed group [29].

Prebiotics and Allergies

There is mounting evidence that the pathogenesis of several inflammatory illnesses is influenced by the gut microbiota. There is currently interest in research examining the variations in the gut microbiota of infants who are atopic and those who are not. The question of whether a particular makeup of the early gut microbiota precedes the later development of atopic sensitization was examined by Kalliomäki et al. [30]. At three weeks and three months of age, they examined the intestinal flora of infants who were at high risk of developing atopy. If the infants had at least one positive skin prick test by the time they were 12 months old, they were categorized as atopic. The findings showed that compared to non-atopic infants, those who had atopy at 12 months had fewer bifidobacteria and more clostridia in their stools at 3 weeks. As a result, it was proposed that a higher prevalence of bifidobacteria was linked to immune function maturing towards a non-atopic condition [30].

One potential intervention strategy for avoiding allergy diseases is the use of prebiotic supplements. Evidence-based guidelines from the ESPGHAN Committee on Nutrition and the World Allergy Organization guideline panel propose prebiotic supplementation as a prophylactic allergy intervention for infants who are not breastfed exclusively. However, as breast milk already contains a significant amount of prebiotics in addition to other beneficial components, this is not the case for infants who are exclusively breastfed [31].

utilizing the scoring atopic dermatitis index, one study evaluated the effectiveness of utilizing FOS as a prebiotic in treating eczema in a small, placebo-controlled study. After 6 and 12 weeks of treatment, the authors of this study found that the eczema median scores were considerably lower than those of the placebo group [32].

In the first two years of life, supplementing with a prebiotic mixture (8 g/L of scGOS/lcFOS) significantly lowers the incidence of allergic manifestations, including recurrent wheezing, atopic dermatitis, and allergic urticaria, according to another dietary intervention study by Arslanoglu et al. [33]. These effects were observed to persist even after the intervention was over, indicating that the prebiotic mixture had a long-lasting immune-modulating effect [33].

Before prebiotics can be recommended as a routine method for allergy prevention in formula-fed infants, more thorough testing is necessary. This is the conclusion reached by the majority of meta-analyses and systematic reviews in this field, despite the fact that studies have shown that prebiotic use can positively impact allergic manifestations. The numerous other potential causes of allergy development are partly to blame for this. [34]

Prebiotics and Infections

Several studies, including randomized controlled trials (RCTs), have demonstrated that supplementing infant milk formula with a particular oligosaccharide composition (GOS/FOS) significantly increases the number of bifidobacteria and decreases the number of pathogens, including *E. coli*, clostridium, and eubacteria, in infants and older children when compared to a group of infants fed a supplemented formula. Additionally, they produce stools that resemble those of babies who are given human milk, indicating improved gastrointestinal tolerance. However, these effects may be dose dependent, with higher dosages producing better outcomes. Nevertheless, it is still unclear and debatable whether these data have any clinical significance [35].

In a 6-month RCT, oligosaccharide prebiotics were also found to dramatically lower the risk of recurrent infections, especially respiratory ones, during the first six months of life, as well as the frequency of infectious episodes (gastrointestinal and respiratory infections). It was hypothesized that the primary cause of the observed early-life preventive mechanism is the immune-modulating effects of the prebiotic combination through changes in the intestinal flora [36].

Prebiotics and Inflammation

The dysbiosis between disease-causing and protective gut flora, which causes and maintains chronic inflammation of the colon and other extra-intestinal organs, is one example of a potential environmental trigger that prebiotics help to rectify. Prebiotics have been demonstrated to help reduce inflammation by specifically promoting the growth of beneficial microbes like *Bifidobacterium* and strengthening resistance to colonization with bacteria that cause disease, such as *Bacteroides* spp. In some animal models of colitis, certain prebiotics have been shown to be helpful. In a few small, controlled studies, prebiotics, either alone or in combination with probiotics, improved certain inflammatory bowel disease (IBD) markers in humans. Although encouraging, there were not enough patients included in these studies to allow for the drawing of any firm conclusions. Nevertheless, the aforementioned results are highly instructive and continue to be the subject of further carefully planned research on the application of prebiotics in IBD. [37]

Prebiotics and Functional Gastrointestinal Disorders

The description and categorization of functional gastrointestinal diseases in children have advanced significantly, although the cause is still unknown. Despite being a very prevalent functional problem among early newborns, infantile colic is still not well understood. Recent research has linked changes in gut microbiota to colic by affecting gut motility, which in turn affects gaseous output and, consequently, excessive crying. In particular, there is growing evidence that infants with colic have a less varied microbiome and fewer bifidobacteria and lactobacilli than controls [38].

Savino et al. [39] conducted observational research on 214 newborns with colic up to three months of age. They found that 79% of children who were given a formula that contained 90% ScGOS, 10% Lc-FOS, sn-2 palmitic acid, and partially hydrolyzed proteins had a lower incidence of colic. Prebiotics have been shown

in most related research to raise the ratio of bifidobacteria to total fecal bacteria, soften stools, and increase stool frequency without diarrhoea when taken in adequate levels [40].

Supplementing with inulin-type fructans (which comprise 70% oligofructose and 30% IcFOS) improved stool consistency, frequency, and texture over time to a softer consistency in a randomized controlled trial. This result was in line with other research on both adults and infants, and it raises the possibility that using prebiotics instead of laxatives to treat constipation could decrease its incidence. A more recent systematic review, however, was unable to find sufficient evidence to support the use of prebiotics to alleviate constipation. The fact that constipation can be caused by a wide range of different reasons is a reasonable explanation for the lack of suggestion. [41]

There are no published randomized controlled trials examining the impact of prebiotics in children with functional abdominal discomfort or irritable bowel syndrome. It is challenging to draw any firm conclusions from the two paediatric studies that examine the effects of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols on children because neither group examined the long-term positive effects and neither group had statistical validation. [41]

Prebiotics and Infantile Colic

Compared to earlier studies on probiotics and synbiotics, there is a dearth of information on the use of prebiotics to alleviate newborn colic. 94 intermediate or late preterm children were randomly assigned to receive a probiotic (*Lactobacillus rhamnosus* GG ATCC 53103) or a prebiotic mixture of GOS and polydextrose or a placebo during the first two months of life and followed up for a year in Finnish randomized double-blind research. 27 out of 94 babies (29%), and the prebiotic and probiotic groups had excessive crying at considerably lower rates than the placebo group (19% vs. 19% vs. 47%, respectively; $p = 0.02$). [42]

It is currently not possible to provide broad guidelines about the use of any particular prebiotic in infancy as a preventative or therapeutic treatment for infantile colic. Prebiotics are not advised for usage as a preventative or treatment measure for infantile colic.

Prebiotics and Acute Infectious Diarrhea

Compared to previous experience and research with probiotics and synbiotics, there is less evidence available regarding the use of prebiotics to treat acute infectious diarrhoea in children. Three randomized controlled trials are looking into how prebiotics affect diarrheal illness.

Hoekstra et al. [43] evaluated the safety and efficacy of a combination of nondigestible carbohydrates (including soy polysaccharide 25%, alpha-cellulose 9%, gum arabic 19%, FOS 18.5%, inulin 21.5%, and resistant starch) in 144 boys with mild to moderate dehydration associated with diarrhoea who were aged 1–36 months in Egypt, Greece, Israel, Italy, Holland, Poland, Portugal, and Slovenia. The 48-hour stool volume, length of hospital stays, and diarrhoea duration did not change between the prebiotic and placebo groups.

In order to evaluate the benefits of a polyphenol-based prebiotic in 111 children and 133 adults who had symptoms of acute gastroenteritis, specifically mild to moderate diarrhoea, Noguera et al. [44] conducted a double-blinded RCT in Nicaragua. The length of time until the last unformed stool was the main goal of this investigation. The current study found that at different time intervals, such as 30 minutes, 2 hours, 24 hours, 48 hours, 72 hours, and 5 days, people who received prebiotic treatment had significantly shorter times until their last unformed bowel movement. Furthermore, a significant reduction in acute gastroenteritis symptoms was seen. However, it is important to note that no subgroup analysis was conducted specifically for children, and the trial excluded all participants under the age of 12 due to safety concerns.

In Italy, 119 infants with severe diarrhoea, ages 3 to 36 months, participated in a single-blind, prospective, controlled RCT by Passariello et al. [45]. They investigated the efficacy of a hypotonic oral rehydration solution (ORS) containing zinc and prebiotics (FOS and xylooligosaccharide) in treating children's acute diarrhoea. When children took ORS along with zinc and prebiotics, their diarrhoea resolved much more quickly after 72 hours. Despite the positive results of this trial, it is impossible to rule out the impact of zinc in the prebiotic arm.

It was difficult to assess the effectiveness of the intervention and offer a recommendation because there were not at least two RCTs that assessed the identical prebiotic preparation. Prebiotics are not advised to be used in the treatment of acute infectious diarrhoea.

Prebiotics and Helicobacter Pylori Infection

Proton pump inhibitors and antibiotics are part of the *H. pylori* treatment regimen, and they may be linked to dysbiosis. In order to avoid difficulties, there may be theoretical justifications for using long-term strategies, like administering prebiotics, to target the intestinal flora. Additionally, using certain probiotics may help avoid antibiotic-induced diarrhoea and boost *H. pylori* eradication rates. [46] However, neither in children nor in adults with *H. pylori* infection have prebiotics as such been studied in randomized controlled trials. The *H. pylori* Special Interest Group of ESPGHAN recently reviewed the treatment of *H. pylori* infection in European children, but they made no mention of prebiotics. [47]

Prebiotics are not advised for the prevention or treatment of *Helicobacter pylori* infections.

Prebiotics and Functional Abdominal Pain Disorders (Fapd)

A meta-analysis and systematic review conducted in 2022 found six research assessing the use of prebiotics in treating childhood FAPD. [48] Three studies looked at children who met the Rome II, III, and IV criteria for irritable bowel syndrome (IBS). 71 children aged 4 to 16 who had been diagnosed with IBS based on Rome III criteria were involved in the randomized, double-blind, controlled, and prospective trial from Türkiye. When compared to prebiotics, the administration of synbiotics and probiotics produced notable improvements in constipation, bloating after meals, and belching-abdominal fullness. [49] In the second study, a double-blinded randomized controlled trial from the United States, the mean number of pain episodes was reduced after 4 weeks of psyllium intake compared to a placebo (8.2 ± 1.2 vs. 4.1 ± 1.3 , $p = 0.03$). Although there was a decrease in the average number of pain episodes, there was no difference in the severity of the pain, the total number of episodes, or other factors between the groups. [51] Another double-blind randomized controlled trial from India examined how four weeks of psyllium prebiotic treatment affected the IBS severity scoring scale (IBS-SSS). At four weeks, the psyllium group's IBS-SSS was significantly lower than that of the placebo group ($p < 0.001$). In a similar vein, remission was achieved by 43.9% of the psyllium group compared to 9.7% of the placebo group. [51] Despite some intriguing findings, there aren't many studies on psyllium, and more carefully planned randomized controlled trials are required.

Another RCT from Poland assessed the impact of giving 84 participants with functional gastrointestinal disorders (FGIDs) associated with stomach pain glucomannan supplements for four weeks. They came to the conclusion that glucomannan was no more successful than a placebo in treating children's FGIDs. [52] In Italy, an RCT involving 60 children examined the impact of partly hydrolyzed sugar gum supplementation on FAP and IBS in comparison to a placebo. When compared to the placebo group, the supplemented group demonstrated greater efficacy in reducing clinical symptoms and improving the Birmingham IBS score ($p = 0.025$). The Wong-Baker Face Pain Rating Score was used to measure the intensity of abdominal pain in FAPD, and the results showed an improvement in pain (40% vs. 13.3%, $p = 0.025$). Two more studies that looked at the effect of prebiotics on functional gastrointestinal problems in both healthy children and autistic people without a specific diagnosis of either FAPD or IBS were excluded from this analysis. [53, 54]

In summary, two RCTs showing the therapeutic effectiveness of psyllium supplementation in kids with IBS were found. For kids with irritable bowel syndrome, doctors might suggest taking supplements of psyllium.

Prebiotics and Functional Constipation

The authors stated that the investigated treatment (dietary fiber, prebiotic mixtures of transgalactooligosaccharides, inulin, soy fiber, or resistant starch) was just as effective as lactulose on fecal incontinence, abdominal pain, frequency of defecation, or stool consistency, but they did not define treatment success. [55] Defecation frequency was recorded, and no statistically significant differences were observed between the investigated products and laxative therapy, placebo, or another control treatment [51]. In terms of safety, a number of studies documented adverse events, and some noted moderate side effects in the experimental group, including vomiting, flatulence, diarrhoea, and stomach distention. [56, 57]

It is not possible to establish a strong and noteworthy effect of prebiotics as adjuvants in the full treatment of functional constipation due to the quality of the data. The use of prebiotics for functional constipation is not advised.

Prebiotics and Inflammatory Bowel Disease (Ibd)

It has been discovered that diets high in fruits, vegetables, and fiber—which are rich in chemicals with prebiotic qualities—have a protective effect against IBD. [58] As a result, prebiotics may be a useful adjunctive therapy for bringing about and maintaining remission in IBD patients. Prebiotic usage in IBD patients, particularly in the adult population, has, however, received little attention in the literature. [59] There were no studies on children. Thus, it is impossible to draw any conclusions on the value of prebiotics for kids with IBD.

The use of prebiotics in people with inflammatory bowel disease is not advised.

Prebiotics and Allergy

Evidence-based recommendations for primary prevention are required due to the high frequency of allergy disorders in Western nations and the limited potential for causative therapy. [60] Prebiotics' potential as an effective allergy prevention method is being highlighted by the growing recognition of the role that early nutrition and gut microbiota play in regulating the immune system's optimal development and function. [61] According to preclinical and clinical research, certain prebiotics may help prevent the development of allergic diseases by influencing the structure and function of the gut microbiome in a positive way. They may also directly interact with immune and epithelial cells to control the structure and function of the gut barrier and the immune system's response to environmental antigens. [62] Prebiotic supplements may reduce allergic reactions and promote immunological tolerance in mouse models, according to the majority of preclinical data. [63] Studies assessing individuals at risk for allergies and the few available research on prebiotic supplements in expectant and nursing mothers provide the basis of clinical evidence. Furthermore, atopic dermatitis (AD) has been the focus of the majority of clinical trials assessing the preventive effect of prebiotics against allergies, while other allergic illnesses have received far less attention. [64] Lastly, the EAACI recommendation states that the present standards do not advise using prebiotics in infant formula or even for the avoidance of allergies. However, the prebiotic intervention has an excellent general safety profile, and several trials assessing its ability to prevent allergies did not find any negative side effects. A noticeably increased incidence of allergic rhinitis was discovered as a side effect in intervention research detailing the allergy-preventive impact of prebiotics in AD. [60]

Prebiotics are not advised for the prevention of atopic dermatitis, asthma, allergic rhinitis, or food allergies.

Chapter Three: Methodology

Study Design

This was a cross-sectional, case-control study using interviewer-administered questionnaires to survey prebiotic use in children with Gut disease.

Participants

The Maternity and Children Hospital Makkah - Makkah Health Cluster was the recruitment site for participants. After attending outpatient clinic, 30 patients with gut disease and on prebiotics were questioned, while healthy controls were those who regularly attended clinics with gut disease and not on prebiotics.

There were participants that are 18 years of age or younger. A verified diagnosis of the illness was the criterion for inclusion for patients with gastrointestinal disorders. Attendance at the hospital outpatient clinic was the inclusion criterion for healthy controls. If participants in either group had a serious medical condition other than the one, they were receiving treatment for at the clinic where they were recruited, they were eliminated from the study. Any medical, surgical, or psychiatric problem requiring ongoing care, whether now or in the past, was considered a major health condition. Any symptoms or diagnosis related to the gastrointestinal system with prebiotics use were considered a control. Cohorts with comparable demographic backgrounds can be recruited by enlisting healthy controls from outpatient clinics housed in the same hospitals as the patients with gastrointestinal diseases.

Questionnaire

On the day of their clinic visit, patients finished the research. Trained researchers conducted in-person interviews using the questionnaire. Interviews took place in hospital private rooms. The same Dietitian has supervised the researchers throughout their first interviews to guarantee consistency and objectivity. The researchers also received interview style training. Standardized terminology and a predetermined order of questioning were employed. To be sure that any disparities between all patients cannot be the result of differences in how the questions were administered and interpreted by different interviewers, researchers interviewed all cases.

The first part included clinical data, such as medical history, and demographic data, such as region of practice, age and gender. The use of prebiotics and how they help to alleviate GIT symptoms was covered in the second part. From a list, participants were asked to choose the prebiotics they utilized. Additionally, details about when the medication was used (recently, last month, last year, or more than a year ago), why it was used, how much was used, how often it was used, how long it caused side effects, how satisfied the user was with the medication, and whether it was used in addition to or instead of traditional medical treatment (alternative or complementary).

Statistics

By dividing the total number of patients who report using prebiotics by the total number of respondents, the prevalence of use was determined. Descriptive statistics were used to analyze the illness and demographic variables. The chi-squared test was used to compare categorical data between participants; Fisher's exact tests were employed if more than 25% of the cells had counts lower than 5. A t-test or the Mann-Whitney U and Kruskal-Wallis tests, depending on whether the data was parametric or nonparametric, were used to compare continuous data between participants. Unless otherwise indicated, continuous data are presented as mean (SD). Microsoft® Excel® for Microsoft 365 MSO (Version 2411 Build 16.0.18227.20082) R software, version 4.4.1 was used.

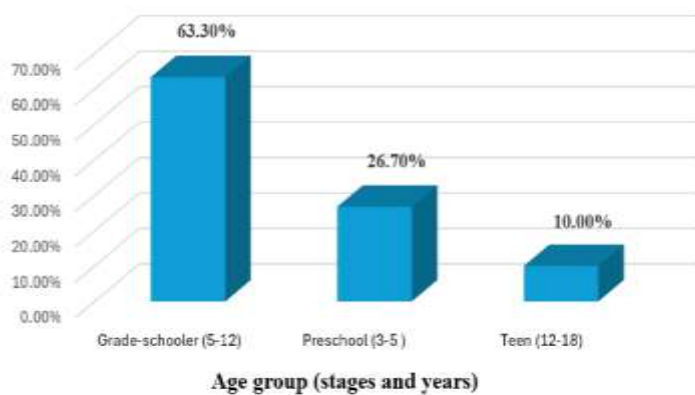
To ascertain the effects of prebiotic use, binary logistic regression analysis (forward likelihood ratio approach) was carried out. The odds ratio (OR; 95% confidence interval [CI]) was used to quantify the degree of correlation between the usage of prebiotics and improved health result.

Ethical Considerations

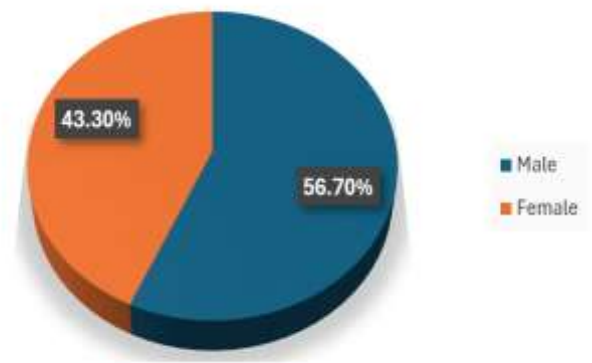
Before the interview ends, informed consent was given to each participant. There were no medical or dental team members present throughout the interview process, nor the interviewers were part of the team providing the participant's care. Questionnaires were anonymized, and all interviews were kept private.

Chapter Four: Results

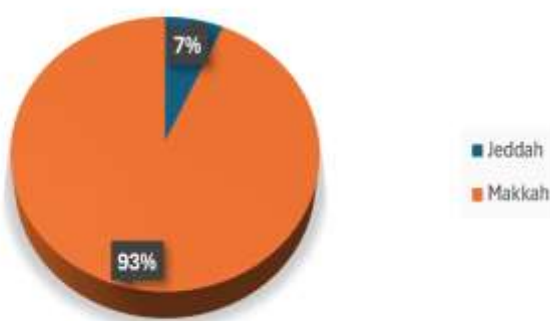
**Age of participants
Frequency (%)**



Gender



**Region of practice
Frequency (%)**



**Medical history
Frequency (%)**

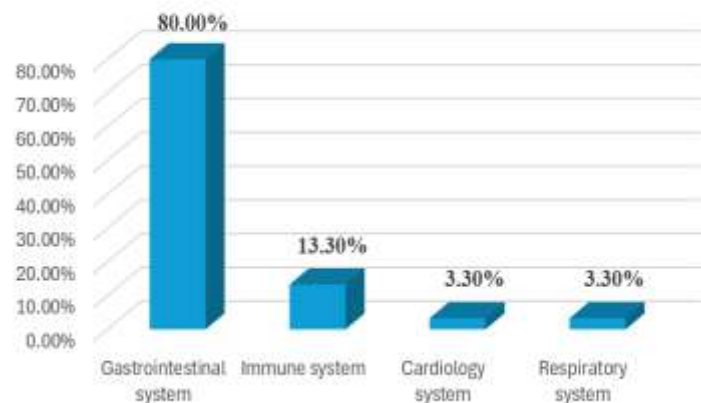


Figure 4.1 Medical History and Sociodemographic Variables.

The survey data revealed that most participants were male (56.7%), while females accounted for 43.3% of the sample. Regarding age distribution, the largest proportion of participants (63.3%) belonged to the grade-schooler group (5–12 years), followed by preschool-aged participants (3–5 years) at 26.7%. Participants in the teen group (12–18 years) represented the smallest percentage at 10.0%. Concerning the region of practice, most participants reported practicing in Makkah (93%), while a smaller percentage practiced in Jeddah (7%).

In terms of medical history, gastrointestinal system issues were the most frequently reported, comprising 80.0% of responses. Conditions related to the immune system accounted for 13.3%, while the cardiology system and respiratory system were each reported by 3.3% of participants. These findings emphasize the predominance of male participants and younger age groups, with gastrointestinal system issues being the most frequently reported medical condition (Figure 4.1).

Table 4.1 Descriptive Statistics for the Use of Prebiotics and How They Help To Alleviate GIT Symptoms of Frequency (N, %) and the Chi-Square Test.

Questions	Tablets		Powders		Capsule		Syrup/drops		Chi-square		
	n	%	n	%	n	%	n	%	p-Value		
What is the prebiotic did you utilize?	2	6.7	6	20	2	6.7	20	66.7	< 0.001 ***		
Questions	Recently		Last month		Last year		Chi-square				
	n	%	n	%	n	%	p-Value				
When was the medication used?	13	43.3	13	43.3	4	13.3	> 0.05				
Questions	Prevention purposes during an antibiotic treatment		Improved digestion		Improved GI immunity		Reduce bloating		Reduce allergic conditions		Chi-square
	n	%	n	%	n	%	n	%	n	%	p-Value
Why was prebiotic used?	11	36.7	9	30	2	6.7	5	16.7	3	10	< 0.05 *
Questions	3 grams per day		Less than 3 grams per day		More than 3 grams per day		Chi-square				
	n	%	n	%	n	%	p-Value				
How much prebiotic was used?	16	53.3	10	33.3	4	13.3	< 0.05 *				
Questions	Gas		Bloating		Constipation		Thirst		Chi-square		
	n	%	n	%	n	%	n	%	p-Value		
What are the side effects prebiotic caused?	14	46.7	5	16.7	5	16.7	6	20	> 0.05		
Questions	One day		A few days		Much longer		Chi-square				
	n	%	n	%	n	%	p-Value				
How long prebiotic caused side effects?	4	13.3	24	80	2	6.7	< 0.001 ***				
Questions	Partially satisfied		Fully satisfied		Chi-square						
	n	%	n	%	p-Value						
How satisfied the user was with the medication?	11	36.7	19	63.3	> 0.05						
Questions	In addition		Instead		Chi-square						
	n	%	n	%	p-Value						
Was prebiotic used in addition or instead of traditional medical treatment?	13	43.3	17	56.7	> 0.05						

* Significant at $p < 0.05$, *** Highly significant at $p < 0.001$.

Table 4.1 provides a comprehensive analysis of participants' experiences with prebiotic use, highlighting significant differences in responses across several categories. Chi-square tests revealed statistically significant variations in some areas ($p < 0.001$ and $p < 0.05$), while other categories showed no significant differences ($p > 0.05$), indicating varied patterns of prebiotic use and participant experiences.

Regarding the forms of prebiotics used, the majority of participants (66.7%) opted for syrups or drops, followed by 20.0% who used powders. A smaller proportion of participants (6.7%) used tablets, and another 6.7% chose capsules. These findings suggest a preference for liquid forms of prebiotics, with powders and tablets being less common. When considering the reasons for prebiotic use, the most frequent rationale was as a preventive measure during antibiotic treatments (36.7%), followed by digestive enhancement (30.0%). Other reasons included reducing bloating (16.7%), enhancing gastrointestinal immunity (6.7%), and alleviating allergic conditions (10.0%). Statistically significant differences in the purposes for prebiotic use were observed ($p < 0.05$), highlighting diverse motivations for their consumption.

In terms of the quantity of prebiotics consumed, over half of the participants (53.3%) reported using 3 grams per day. A smaller group (33.3%) used less than 3 grams per day, and only 13.3% exceeded the 3 grams per day threshold. Chi-square analysis showed a statistically significant difference in the distribution of prebiotic usage across these categories ($p < 0.05$), suggesting a tendency for participants to prefer a moderate daily intake. Participants also reported various side effects. The most common side effect was gas (46.7%), followed by thirst (20.0%), bloating (16.7%), and constipation (16.7%). Most side effects were temporary, with 80.0% of participants reporting them lasting only a few days. A smaller group (13.3%) experienced side effects for a single day, and 6.7% reported prolonged effects. No significant differences were found regarding the duration of these side effects ($p > 0.05$).

Regarding satisfaction with prebiotic use, 63.3% of participants expressed full satisfaction, while 36.7% were partially satisfied which no significant differences was shown ($p > 0.05$). Additionally, 56.7% of participants indicated they used prebiotics as a replacement for conventional medical treatments, while 43.3% used them in conjunction with traditional treatments. These findings were statistically significant ($p < 0.001$), underscoring the high level of satisfaction among users and a notable preference for replacing conventional medical interventions with prebiotics. These results highlight the variability in prebiotic use and the diverse experiences of participants, underscoring the need for targeted educational efforts to enhance public understanding of the benefits, appropriate use, and potential side effects of prebiotics.

Efficacy of Prebiotics on Patients with GI Disorders

A Fisher's exact test was conducted to determine whether the method of prebiotic use ("instead of" or "in addition to" traditional treatments) influenced user satisfaction in the management of gastrointestinal (GI) disorders. The analysis compared the distribution of "fully satisfied" and "partially satisfied" users across the two groups.

In the "instead" group, 76.5% of users (13 out of 17) reported being fully satisfied, while 23.5% (4 out of 17) were partially satisfied. In the "in addition" group, 42.9% of users (3 out of 7) reported being fully satisfied, while 57.1% (4 out of 7) were partially satisfied.

The Fisher's exact test showed no statistically significant association between the method of prebiotic use and satisfaction levels ($p = 0.167$; odds ratio = 4.04; 95% CI: 0.47–41.53). These results indicate that there is no strong evidence to suggest that using prebiotics instead of traditional treatments is more effective than using them in addition to traditional treatments in improving user satisfaction for managing GI disorders.

A Welch's two-sample t-test was conducted to examine whether the method of prebiotic use ("instead of" or "in addition to" traditional treatments) influenced user satisfaction in the management of gastrointestinal (GI) disorders. The analysis compared the mean satisfaction scores between the two groups.

In the "instead" group, the average satisfaction score was 2.76 (on a scale where 3 represents "fully satisfied" and 2 represents "partially satisfied"), while in the "in addition" group, the average satisfaction score was 2.43.

The t-test showed that there was no statistically significant difference in satisfaction scores between the two groups ($t = 1.47$, degrees of freedom = 9.49, $p = 0.173$). The 95% confidence interval for the difference in

means was between -0.18 and 0.85, indicating that the true difference in satisfaction scores could range from a slight negative difference to a slight positive difference.

These results suggest that there is no strong evidence to support that using prebiotics instead of traditional treatments leads to higher satisfaction compared to using them in addition to traditional treatments for managing GI disorders.

A logistic regression model was used to evaluate whether using prebiotics alone or in addition to traditional treatments achieves higher efficiency in managing gastrointestinal (GI) disorders. The model included treatment method, age, and gender as predictors.

The model demonstrated adequate fit, with an AIC of 36.37 and a residual deviance of 26.37 on 19 degrees of freedom. Its classification accuracy was 71%, and the area under the receiver operating characteristic (ROC) curve (AUC) was 0.74, indicating fair discriminative performance.

Table 4.2 Logistic Regression Results for Satisfaction with Treatment Methods for Gastrointestinal Disorders

Variable	Estimate	Std. Error	z-value	p-value	Odds Ratio (OR)	95% CI for OR
Intercept	2.4958	1.3405	1.862	0.063	12.13	1.34–348.49
Treatment (In addition)	-1.5584	1.0538	-1.479	0.139	0.21	0.02–1.56
Age (Grade-schooler)	-1.4753	1.3257	-1.113	0.266	0.23	0.01–2.31
Age (Teen)	-1.0222	1.7949	-0.569	0.569	0.36	0.01–15.61
Gender (Female)	-0.4354	0.9820	-0.443	0.658	0.65	0.09–4.86

Regarding treatment methods, the odds of satisfaction with the combined use of prebiotics and traditional treatments were lower compared to using prebiotics alone (OR = 0.21, 95% CI: 0.02–1.56, $p = 0.139$). Although not statistically significant, this trend suggests that prebiotics alone may be more efficient in achieving higher satisfaction levels.

Age and gender did not significantly impact satisfaction. Compared to adults, grade-schoolers (OR = 0.23, 95% CI: 0.01–2.31, $p = 0.266$) and teenagers (OR = 0.36, 95% CI: 0.01–15.61, $p = 0.569$) exhibited lower odds of satisfaction. Similarly, female participants had lower odds of satisfaction than males (OR = 0.65, 95% CI: 0.09–4.86, $p = 0.658$).

The confusion matrix revealed that the model correctly classified 14 satisfied participants and 3 dissatisfied participants while misclassifying 7 cases.

The logistic regression analysis does not show a statistically significant difference between prebiotics alone and their combined use with traditional treatments. However, the observed trend suggests a potential preference for prebiotics alone.

Amount or percentage of side effects that appear and the most common side effect

Frequency of Side Effects

The reported side effects among the 24 participants of GI disorders are summarized below:

Side Effect	Frequency	Percentage of Total Sample
Gas	11	45.8%
Bloating	2	8.3%
Constipation	5	20.8%

Thirst	6	25%
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The most common side effect was gas, reported by 45.8% of participants. The least common side effect was bloating (8.3%).

Side Effects by Prebiotic Intake Method

The following table summarizes the distribution of side effects based on whether the prebiotic was used instead of or in addition to traditional treatments:

Side Effect	Instead (n=24)	In Addition (n=24)	Total
Gas	9 (39.6%)	2 (8.3%)	11
Bloating	1 (4.2%)	1 (4.2%)	2
Constipation	2 (8.3%)	3 (12.5%)	5
Thirst	5 (20.8%)	1 (4.2%)	6

The most notable finding was that **gas** was reported predominantly by participants using prebiotics *instead of* traditional treatments (9 out of 11 participants). In contrast, only 2 participants reported **gas** when prebiotics were used *in addition to* traditional treatments.

For **bloating**, the frequency was low, with only 2 participants reporting this side effect, evenly split between the two intake groups. Similarly, **constipation** appeared more frequently among those using prebiotics *in addition to* traditional treatments (3 out of 5 participants). **Thirst** was reported more frequently in the *instead* group, with 5 out of 6 participants experiencing this side effect.

A **Chi-square test** was conducted to determine whether the method of prebiotic use (instead of or in addition to traditional treatments) influenced the occurrence of side effects in individuals with gastrointestinal (GI) disorders. The analysis compared the distribution of four side effects: gas, bloating, constipation, and thirst across the two groups. The test showed no statistically significant association between the prebiotic intake method and side effects ($X^2 = 3.8173$, $df = 3$, $p = 0.2819$). These results suggest that the method of prebiotic use does not significantly affect the occurrence of side effects in individuals with GI disorders.

A **Chi-square test** was conducted to determine whether the prebiotic dosage (3 grams per day, less than 3 grams per day, or more than 3 grams per day) influenced the occurrence of side effects in individuals with gastrointestinal (GI) disorders. The analysis compared the distribution of four side effects: gas, bloating, constipation, and thirst across the three dosage groups. The test showed no statistically significant association between prebiotic dosage and the occurrence of side effects ($X^2 = 5.5101$, $df = 6$, $p = 0.4802$). These results suggest that the prebiotic dosage does not significantly affect the occurrence of side effects in individuals with GI disorders.

A **Fisher's exact test** was conducted to determine whether the method of prebiotic intake ("instead" or "in addition to") influenced the duration of prebiotic use. The analysis compared the distribution of users who reported using prebiotics for "one day," "a few days," or "much longer" across the two intake methods.

The Fisher's exact test showed **no statistically significant association** between the method of prebiotic intake and the duration of use ($p = 0.178$). These results suggest that there is no strong evidence to conclude that prebiotic intake "instead" of or "in addition to" affects the duration of its use.

A **Fisher's exact test** was conducted to determine whether the type of side effect (Gas, Bloating, Constipation, or Thirst) was associated with the duration of prebiotic use. The analysis compared the distribution of users who reported experiencing each side effect for "one day," "a few days," or "much longer."

The Fisher's exact test showed **no statistically significant association** between the type of side effect and the duration of use (**p = 0.670**). These results suggest that there is no strong evidence to conclude that the type of side effect experienced is influenced by the duration of prebiotic use.

Form of responses were made here:

<https://docs.google.com/spreadsheets/d/175X9vtCWwr0N0Y1L3r1jlkjz1sN9Vs7oIeFOmVwva4Q/edit?usp=drivesdk>

Chapter five: Discussion and Conclusion

Prebiotics are substrates that host bacteria preferentially use to provide health benefits. Studies on prebiotics in children are scarcer than those on probiotics. Prebiotic-supplemented infant formula has been used in the majority of research, however there have been very few reports of employing add-on prebiotic supplements to prevent or cure gastrointestinal issues in children. [65]

This was a cross-sectional, case-control study using interviewer-administered questionnaires to survey prebiotic use in children with Gut disease. The Maternity and Children Hospital Makkah - Makkah Health Cluster was the recruitment site for participants. After attending outpatient clinic, 30 patients with gut disease and on prebiotics were questioned, while healthy controls were those who regularly attended clinics with gut disease and not on prebiotics.

The current study aimed to evaluate effect of Prebiotics in Dietary management of pediatric Gut disease.

In the current study, most participants were male (56.7%), while females accounted for 43.3% of the sample. Regarding age distribution, the largest proportion of participants (63.3%) belonged to the grade-schooler group (5–12 years), followed by preschool-aged participants (3–5 years) at 26.7%. Participants in the teen group (12–18 years) represented the smallest percentage at 10.0%. Concerning the region of practice, most participants reported practicing in Makkah (93%), while a smaller percentage practiced in Jeddah (7%). In terms of medical history, gastrointestinal system issues were the most frequently reported, comprising 80.0% of responses. Conditions related to the immune system accounted for 13.3%, while the cardiology system and respiratory system were each reported by 3.3% of participants. These findings emphasize the predominance of male participants and younger age groups, with gastrointestinal system issues being the most frequently reported medical condition.

In a study by Basturk et al., [49] among the 71 patients in the study, constipation-predominant IBS was the most prevalent subtype; the mean age was 10.88 ± 4.38 years, with a range of 4 to 16 years; and the female to male ratio was 1:1. There were twenty-three patients in the synbiotic group, twenty-four in the probiotic group, and twenty-four in the prebiotic group. Regarding age, sex distribution, IBS subgroups, and early complaints, there was no discernible difference between the groups.

In another study by Güemes et al., [66] 433 paediatric specialists in all, 62% of whom were men, answered the study's questionnaire. 78.4% of participants were above 45, with a mean age of 52.5 (9.3) years. Nearly all paediatricians (91.9%) reported using probiotics, prebiotics, or synbiotics, with immune stimulants (80.4%), vitamins and/or minerals (76.2%), and omega-3 fatty acids (75.1%) following closely behind. There were no differences in the use of dietary supplements by paediatrician age, with the exception of immunological stimulants, which were used by a higher percentage of those over 45 than those under 45 (86.2% vs. 69.0%, $P = 0.001$). Additionally, 81.1% of patients chose to combine pharmaceutical treatment with dietary stimulants. Regarding supplementation indications, the following were proposed: probiotics, prebiotics, and synbiotics in conjunction with antibiotics (92.6%) and in the presence of gastrointestinal disorders (91.2%); immune stimulants to improve defenses and prevent colds (87.1%); vitamins and/or minerals to improve nutritional status (74.8%); omega-3 fatty acids to improve attention-deficit hyperactivity disorder (ADHD) symptoms (84.8%) and concentration (80.1%); and phytotherapy to relieve cough and reduce mucus secretion (29.3%). Approximately 10% of participants (54.1%) reported using homoeopathy with their patients.

Also, in a study by Hume et al., [67] 42 participants were randomly assigned to either the prebiotic or placebo group after signing a consent form to take part in the trial. Twenty participants (10 girls and 10 boys) in the prebiotic group and eighteen in the placebo group (7 girls and 11 boys) finished the trial. Sex, height, weight, and BMI score did not significantly differ across groups at baseline.

In the current study, there were varied patterns of prebiotic use and participant experiences. Regarding the forms of prebiotics used, the majority of participants (66.7%) opted for syrups or drops, followed by 20.0% who used powders. A smaller proportion of participants (6.7%) used tablets, and another 6.7% chose capsules. These findings suggest a preference for liquid forms of prebiotics, with powders and tablets being less common. When considering the reasons for prebiotic use, the most frequent rationale was as a preventive measure during antibiotic treatments (36.7%), followed by digestive enhancement (30.0%). Other reasons included reducing bloating (16.7%), enhancing gastrointestinal immunity (6.7%), and alleviating allergic conditions (10.0%). Statistically significant differences in the purposes for prebiotic use were observed ($p < 0.05$), highlighting diverse motivations for their consumption.

Paediatricians primarily employed dietary supplements called synbiotics to alleviate symptoms associated with gastrointestinal infections [68], secondary to antibiotic use [69], and, to a lesser extent, to boost innate immunity [70]. Because physiologically active polysaccharides have an immunomodulatory effect, immune stimulants were utilized. With proven pluripotent biological effects, beta-glucans are among the most researched natural immunomodulators. They can be used for both prevention and treatment of a variety of clinical conditions, including respiratory tract infections [71] and allergy illnesses [72].

In another study by Güemes et al., [66] 39% of participants assessed the powder as fairly acceptable, while 61% said it was extremely acceptable to consume on a daily basis.

In the current study, participants also reported various side effects. The most common side effect was gas (46.7%), followed by thirst (20.0%), bloating (16.7%), and constipation (16.7%). Most side effects were temporary, with 80.0% of participants reporting them lasting only a few days. A smaller group (13.3%) experienced side effects for a single day, and 6.7% reported prolonged effects. No significant differences were found regarding the duration of these side effects ($p > 0.05$).

In a study by Basturk et al., [49] the most frequent complaints were burp (46; 64.8%), bloating after meals (46; 64.8%), and an abrupt urge to void (47; 66.2%). Mucus in the stool was the least frequent complaint (30; 42.3%). In the entire study group, 19 patients (27%), 24 patients (34%), and 28 patients (39%), reported having abdominal pain every day, once a week, or at least three days a month. Furthermore, none of the synbiotic, probiotic, or prebiotic groups experienced any post-treatment side effects, including diarrhoea, constipation, or stomach pain. The 900 mg of inulin they employed in their study did not alleviate any of the initial concerns.

Improvements in IBS symptoms like gas passage and fullness were found in randomized controlled trials involving patients who took fructooligosaccharides and galactooligosaccharides at different doses ranging from 3.5 to 20 g for 4–12 weeks. [73, 74]

Also, in a study by Hume et al., [67] regarding gastrointestinal side effects, during the trial, 70% of individuals in the prebiotic group and 61% of participants in the placebo group reported no change in bloating or flatulence. Flatulence and bloating were mildly elevated in the prebiotic (25%) and placebo (28%) groups for comparable numbers of participants. A moderate increase in bloating and flatulence was noticed by the remaining 5% and 11% of participants in the prebiotic and placebo groups, respectively. Neither group's members reported experiencing a significant increase in bloating or gas.

In the current study, regarding satisfaction with prebiotic use, 63.3% of participants expressed full satisfaction, while 36.7% were partially satisfied which no significant differences were shown ($p > 0.05$). Additionally, 56.7% of participants indicated they used prebiotics as a replacement for conventional medical treatments, while 43.3% used them in conjunction with traditional treatments. These findings were statistically significant ($p < 0.001$), underscoring the high level of satisfaction among users and a notable

preference for replacing conventional medical interventions with prebiotics. These results highlight the variability in prebiotic use and the diverse experiences of participants, underscoring the need for targeted educational efforts to enhance public understanding of the benefits, appropriate use, and potential side effects of prebiotics.

It is crucial to differentiate between "traditionally used" and "well-established used" dietary supplements in the broad category of goods referred to by several names, such as food supplements, natural health products, dietary supplements, or complementary medications. Certain food supplement categories are solely based on what are known as "traditionally used" (specifically, herbal medicinal plants) due to the widespread belief that they are generally healthy and may aid in a child's growth and development, but they lack evidence of efficacy from intervention studies or clinical trials. However, there are a growing number of food supplements that fall under the category of "well-established used" since their safety and effectiveness have been amply demonstrated by relevant clinical research, and their recommendations are grounded in evidence-based medicine. This is why, given the large variety of paediatric supplements on the market, particularly in certain categories, their evaluation must be grounded in science and take into consideration various clinical studies that show the effectiveness of the primary ingredients, dosages, indications, and treatment duration. These recommendations are met by the food supplements, and well-designed and reliable studies that have been published in the literature support their use in paediatrics [75, 76].

In another study by Güemes et al., [66] 52.1% of participants assessed their overall level of satisfaction as "very satisfied," 40.9% as "quite satisfied," and just 7.1% as "moderately" or "slightly satisfied." Additionally, the category of synbiotics had a larger percentage of "very satisfied" people (62.7%) than the categories of immune stimulants (53%), and omega-3 supplements (30.2%) ($P < 0.001$).

Conclusion

Prebiotics are increasingly acknowledged as a viable therapeutic strategy for boosting general health and preventing and treating a variety of illness states in children. Indeed, the positive therapeutic use of prebiotics appears promising given the incredibly low risk of severe side effects, their ease of administration, and their robust ability to affect the makeup and function of the microbiota in the gut and beyond. Prebiotics are becoming a more well-known immunoactive component that might have long-term impacts.

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