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Original Article

Inulin or human milk oligosaccharides in the management of gastrointestinal symptoms in children with autism: a randomised comparative trial

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ABSTRACT

Background: Gastrointestinal (GI) abnormalities are concurrent symptoms that are commonly found in children with autism. They possess a lower overall abundance of beneficial taxa, in the GI microbiota. Prebiotics, such as Inulin & Human milk oligosaccharides (HMO) promote the growth of beneficial bacteria such as Bifidobacteria, in the GI tract and provide numerous health benefits. Therefore, this study was undertaken to compare the beneficial effects of Inulin and Human Milk Oligosaccharides (HMO) in managing gut health issues in autistic children age group 4-10 years.
Materials and Methods: This was an open randomized trail undertaken from December 2022 to May 2023. Sixty children diagnosed with autism with gut-related issues with ROME III criteria were enrolled in the study and randomly divided into two groups. Group A received 1 gram of HMO daily and Group B received 0.8 grams of inulin daily for 12 weeks. Ethical clearance was obtained, and study is registered with Clinical Trial Registry of India. Informed consent was obtained from the parents of the children before enrolment. Data at baseline and at the end of 12 weeks were collected. Total Score between two interventions was analyzed by using student test and comparison of each GI symptoms was done by Mann-Whitney U test. P value less than 0.05 was considered ads significant.
Results: There was significant difference between the mean values of the total scores on ROME Criteria III of Inulin and HMO groups at baseline and at the end of 12 weeks of the intervention ($p < 0.001$*** and $p < 0.001$***, respectively).
Conclusion: HMO showed better outcomes than inulin in the treatment of GI dysfunction in children with autism.

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Introduction

Autism, or autism spectrum disorder (ASD), is the fastest growing neurodevelopmental disorder, characterized by challenges with social skills, restrictive and repetitive behaviours, speech, and nonverbal communication. According to the estimates of the CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network, one of 36 children has been identified as having autism spectrum disorder (ASD) [1]. In India, it has been estimated that more than 2 million children less than 15 years of age might be affected with autism spectrum disorder. This amounts to huge numbers as they form 1/3rd of the population of the country [2]. Comparing the European data, according to a recent study by Autism Spectrum Disorders in Europe (ASDEU) on the prevalence of autism in 11 Member States, around 1 child in 89 has ASD. Even more alarming, according to the Italian National Institute of Health, the figure is 1 child in 77 in Italy [3]. The Lifetime prevalence of GI symptoms including diarrhoea, abdominal pain and constipation is 70% in autistic population compared to 28% in typically developing children [4]. Children with autism spectrum disorder also develop multiple comorbidities ranging from psychiatric issues to commonly seen gastrointestinal disorders. The gut micro biota is crucial for optimal health and plays a vital role in important metabolic, protective, and trophic functions. It has often been referred to as the "forgotten organ" in the literature [5].

Immune system dysfunction is a well-known issue in ASD, possibly driving the dysbiotic microbiota, or alternatively created by it. The relationship between dysbiosis and the high incidence of comorbid GI dysfunction in ASD is not well elucidated; however, the studies reviewed by Hughes, et. al indicate that a relationship exists. Reports that behaviours improve after modification of the microbiota support the hypothesis that dysbiotic microbiota, their influence on the immune system, and their metabolic byproducts contribute directly to the development of these disorders [6].

Gut microbiome alterations probably due to altered gut microbial components are implicated in ASD. The species that have been reported to change include higher concentrations of pathogenic *Clostridium* bacteria, decreased *Bacteriodes:Firmicutes* ratio, and increased *Desulfovibrio* species. This leads to the translocation of bacteria and their antigens, toxins, and metabolites. These derangements become more profound during the administration of antibiotics, and reversal of these GI and behavioral symptoms are also reported after antibiotics are stopped [7-9]. This opens up further avenues of research on the role of gut microbiota-altering agents such as prebiotics and probiotics as a potential therapeutic option. In recent years, considerable attention has been paid to the bidirectional relationship between the gut and the brain, linking emotional factors and various cognitive centers in the brain with functions of the intestines, and gut microbiota has been reported to play an important role in modulating the gut–brain axis (GBA) [10-11]. A few studies have reported that probiotics and prebiotics are able to alleviate GI symptoms as well as improve behavioral issues in children with ASD [12-14]. The most studied prebiotics are the soluble fibres inulin, fructo-oligosaccharides (FOS), galactooligosaccharides (GOS), and more recently, human milk oligosaccharides (HMOs). Human Milk Oligosaccharides (HMO) are among the main components of breast milk. It is associated with functional development during early life, immunity, and GI health through various mechanisms. Inulin is a prebiotic composed of plant sugars linked in chains or processed. They are found in beans, certain cereals, plants of the Allium family, and root vegetables. Studies have reported that HMO enhances gut health by building up and supporting colonies of beneficial bacteria such as lactobacilli and Bifidobacter, while inulin promotes the growth of both beneficial and non-beneficial bacteria [15-17]. Both are reported to be beneficial in treating GI complaints in autistic children. Therefore, this study aimed to compare the effects of HMO and inulin in managing gut issues in children with autism.

Objectives of the Study

To evaluate and compare the effects of Inulin and Human Milk Oligosaccharides (HMO) from baseline to the end of 12 weeks in managing gut issues in children with autism aged 4 -10 years.

Material and Methods

This was an open randomized open trial undertaken by the Giggles Clinic, Delhi, from December 2022 to May 2023. Children aged group 4 -10 years diagnosed with autism with gut-related issues who visited the clinic during the study period were screened according to eligibility criteria and were then enrolled in the study. A Rome III criterion for functional gastrointestinal disorders was used to assess gut-related issues in children with ASD [18]. The enrolled patients were divided randomly into two groups. Randomization was performed using a computer-generated random sequence number and placed in opaque sealed

envelopes. Sixty children were enrolled and randomly divided into two groups, with 30 members in each group. Informed consent was obtained from the parents of the children before enrolment. Written informed consent was obtained from the parents of the enrolled children, and assent was obtained from children above the age of 7 years. Ethical clearance was obtained by Institutional Ethical Committee, IDS, UP via Ref no: IEC/60A/2022.The data was collected by trained nursing staff at the Giggles Clinic in Delhi. This study is registered with Clinical Trial Registry of India (CTRI) with Ref No CTRI/2022/12/048212 dated 19th December 2022.

Eligibility Criteria

Inclusion Criteria: Children between 4-10 years diagnosed with autism having gastrointestinal problems fulfilling Rome III criteria for functional gastrointestinal disorders were included in the study.

Exclusion Criteria: All children having gastrointestinal problems other than autism were excluded.

Grouping

Group A received HMO: Pure HMO for children powder containing 800 mg 2' fucosyl lactose per serving and Lacto-N-neotetraose 200 mg per serving. The dose given was 1.0 gm daily (as prescribed by the manufacturer). It was manufactured by Layer Origin Nutrition, NY (USA) (free from eggs, fish, shellfish, tree nuts, peanuts, and wheat).

Group B received Inulin: Certified Organic Inulin (pure prebiotic powder) 0.9g was administered daily to the study population. The main ingredients included Total carbohydrates 2.7 g/serving, Dietary fiber – 2.5 g/serving, Organic Inulin (FOS) (from Blue agave) (Figure 1).

All the enrolled patients were telephonically reviewed every 15 days to monitor the compliance.

Study Parameters

Abdominal symptoms were included according to the Rome III criteria for functional gastrointestinal disorders (Table 1) [18].

Table 1: Included Abdominal symptoms according to the Rome III criteria.

S. No.	Abdominal Symptom	Details: In the past 2 months, how often did your child experience the following
1	Diarrhoea	a. Passing 1-2 episodes of loose watery stools without smell/day b. Passing episodes of loose watery stools with smell /day c. Passing more than 2 episodes of loose watery stools /day d. Does the diarrhoea last for more than 5 days
2.	Constipation	a. Does the child passes stools comfortably daily without pain and pressure? b. Does the child feel pain/apply pressure while passing stools? c. Does the child complaints of hard lump like stools (consistency of stools) d. Does the child pass stools after every 2 to 4 days (how often does it happen?)
3.	Abdominal Pain	a. Does the pain remain continuous throughout the day? b. Is the pain severe enough to effect his/her daily routine activities (learning, academics, ADL- activities of daily routine.) c. Does the pain come in intervals? (Colicky- does it get worsen after eating meals) d. How often is the belly pain associated with vomiting/reflex issues?
4.	Vomiting/Reflex	a. How often did your child vomit/throw up? b. How often did your child nauseated but did not vomit? c. How often did your child experience burning sensation (c/o pain in the upper chest)? d. How often did your child experience nausea before vomiting
5.	Bloating	a. Burp (belch) again and again without vomiting? b. Pass a lot of gas very frequently? c. Develop a swollen belly during the day (belly that definitely sticks out more than usual)? d. Swollen or gulp extra air? (you might hear a clicking noise when your child swallows)

Interpretation of Scoring System (Table 2)

Table 2: Interpretation of Scoring System.

S. No.	Score System	Score
1	Score 0	Never
2	Score 1	1-3 times in a month
3	Score 2	Once a week
4	Score 3	Several times in a week
5	Score 4	Every day

Statistical Analysis: The data were summarized to test the differences in mean values. Baseline and end scores were compared using the Mann-Whitney U test. The percentage difference from baseline to the end of the 12 weeks was calculated using the Wilcoxon matched-paired test. The data were analyzed using SPSS IBM Corp. Released 2020. IBM SPSS Statistics, for Windows, Version 27.0. Armonk, NY: IBM Corp. Statistical significance was set at $p < 0.05$.

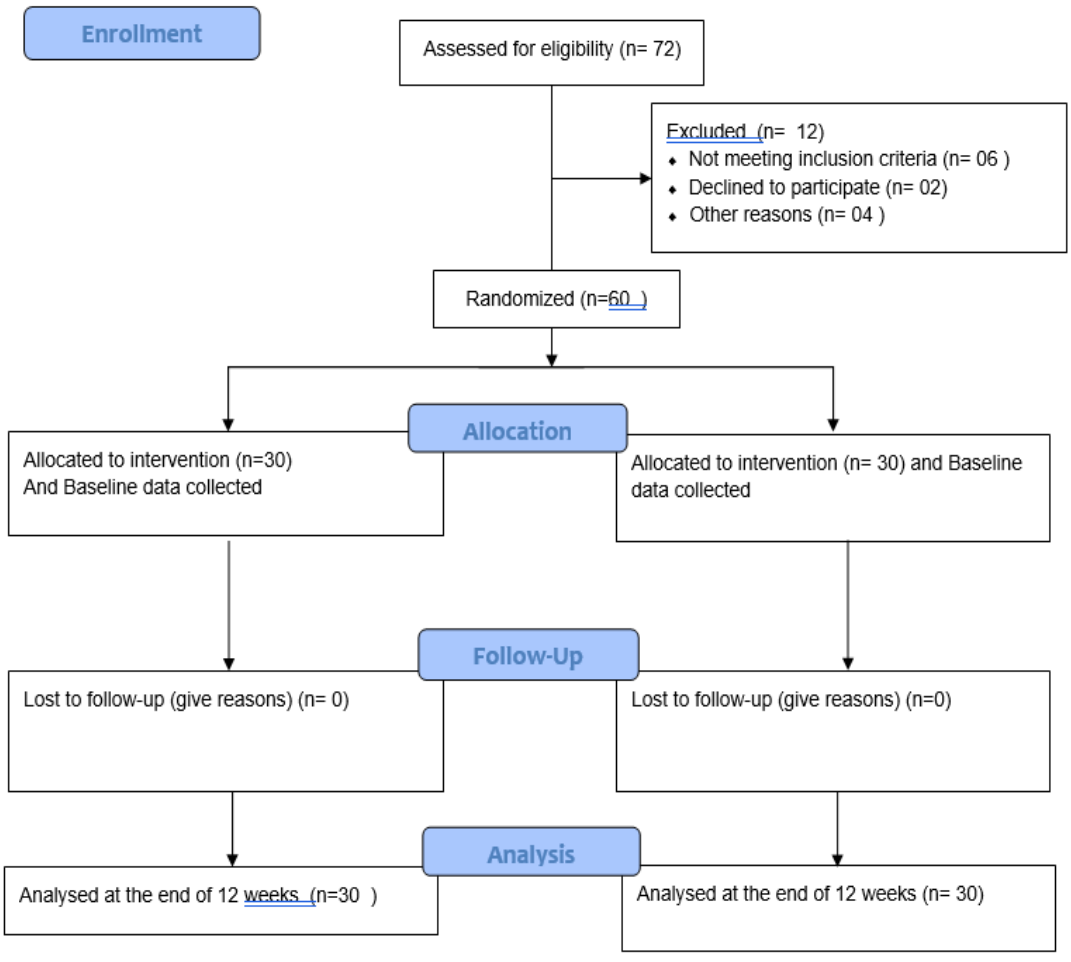

Figure 1: Consort Flow-diagram.

Results

The mean age group was 5.59 ± 1.28 with 61.67% of boys and 38.33% of girls were enrolled. (Table 3). There was a significant difference between the mean values among the Inulin and HMO groups at the baseline and end ($p<0.001$*** and $p<0.001$***, respectively). (Table 4) There was a significant improvement in the following symptoms in the HMO group compared with the inulin group. (Table 5).

Table 3: Demographics of the study participants

	Inulin group	%	HMO group	%	Total	%	Statistic	p-value
Gender								
Boys	17	56.67	20	66.67	37	61.67	χ^2=0.6350	0.4260
Girls	13	43.33	10	33.33	23	38.33		
Age in yrs								
Mean	5.69		5.48		5.59		t=1.7140	0.0920
SD	1.24		1.34		1.28			

The mean age group was 5.59 ± 1.28 with 61.67% of boys and 38.33% of girls were enrolled.

Table 4: Comparison of Total Score on ROME Criteria III among study participants

Test	Prebiotic	Mean ± SD	t- test	Mean diff (95% CI)	p-value
At Baseline	**HMO**	28.43 ± 2.32	4.609	3.033 [1.715 – 4.351]	<0.001***
	Inulin	31.47 ± 2.75			
At end of 12 weeks	**HMO**	16.83 ± 2.93	17.48	12.40 [10.98 – 13.82]	<0.001***
	Inulin	29.23 ± 2.54			

*There was a significant difference between the mean values among the Inulin and HMO groups from the bassline to end of 12 weeks of Intervention ($p<0.001$*** and $p<0.001$***, respectively).*

1. Diarrhoea:
   a. There was a decrease in the mean frequency of passing 1-2 episodes of loose watery stools without smell in the HMO group (1.2±0.4) as compared to the inulin group (2.4±0.7).
   b. There was a decrease in the mean frequency of passing 1-2 episodes of loose watery stools with smell in the HMO group (0.4±0.5) as compared to the inulin group (1.5±0.7).
   c. There was a significant reduction in the duration of diarrhoea lasting for more than 5 days in the HMO group (0.1±0.3) as compared to the inulin group (1.0±0.6).
2. Constipation:
   a. The study participants reported passing stools comfortably daily without pain in both study groups and significantly more in the inulin group (1.5±0.6) as compared to the HMO group (1.9±0.7)
   b. There was a significant improvement in terms of pain and applying pressure in the HMO group (1.5±0.5) as compared to the inulin group (2.1±0.5).
   c. Constipation with regards to formation of hard lumpy stools was better in HMO group (1.4±0.5) as compared to Inulin group (2.1±0.6).
   d. The frequency of children passing stools after 2-4 days was improved significantly in the HMO group (0.7±0.6) as compared to the inulin group (1.3±0.6).
3. Abdominal Pain:
   a. The study participants reported significant improvement in terms of pain affecting daily activities in the HMO group (0.6±0.6) as compared to the inulin group (1.0±0.6) and pain sensation in intervals in the HMO group (0.7±0.7) as compared to the inulin group (1.4±0.5).
   b. The study participants reported significant improvement in terms of abdominal pain associated with vomiting in the HMO group

(1.2±0.7) as compared to the inulin group (1.8±0.6).

4. Vomiting:
   a. There was significant improvement in terms of episodes of vomiting in the HMO group (0.8±1.0) as compared to the inulin group (1.6±0.7), and the feeling of nausea before vomiting in the HMO group (1.1±0.6) as compared to the inulin group (2.0±0.8).
5. Bloating:
   a. The study participants reported significant improvement in symptoms, that is, repeated burps without vomiting in the HMO group (1.3±1.1) as compared to the Inulin group (2.0±0.8), passing gas frequently in the HMO group (0.6±0.8) as compared to the Inulin group (2.2±0.7), and developing a swollen belly during the day in the HMO group (0.8±0.4) compared to the Inulin group (1.8±0.6).

Table 5: Comparison of Inulin group and HMO from the baseline to the end of 12 weeks of the intervention Mann-Whitney U test.

Parameters	Time	Inulin group				HMO group				U-value	Z-value	p-value
		Mean	SD	Median	IQR	Mean	SD	Median	IQR			
1. Diarrhoea												
A: passing 1-2 episodes of loose watery stools without smell / day	Baseline	2.4	0.8	3.0	0.0	2.4	0.9	3.0	0.0	448.50	-0.0148	0.9882
	At the end of 12 weeks	2.4	0.7	3.0	0.0	1.2	0.4	1.0	0.0	77.50	5.4998	0.0001*
B-passing episodes of loose watery stools with smell /day	Baseline	1.4	0.8	1.0	0.5	1.1	0.7	1.0	0.0	342.00	1.5893	0.1120
	At the end of 12 weeks	1.5	0.7	2.0	0.0	0.4	0.5	0.0	0.5	122.00	4.8419	0.0001*
C-passing more than 2 episodes of loose watery stools / day	Baseline	1.1	0.7	1.0	0.5	0.6	0.6	1.0	0.0	305.50	2.1290	0.0333*
	At the end of 12 weeks	1.0	0.7	1.0	0.0	0.6	0.6	1.0	0.0	332.50	1.7298	0.0837
D-does the diarrhoea lasts for more than 5 days	Baseline	1.2	0.6	1.0	0.5	0.6	0.5	1.0	0.0	249.00	2.9643	0.0030*
	At the end of 12 weeks	1.0	0.6	1.0	0.0	0.1	0.3	0.0	0.0	85.00	5.3889	0.0001*
2. Constipation												
A-does the child passes stools comfortably daily without pain and pressure	Baseline	1.4	0.7	1.5	0.3	1.2	0.6	1.0	0.5	377.50	1.0645	0.2871
	At the end of 12 weeks	1.5	0.6	1.5	0.3	1.9	0.7	2.0	0.0	282.00	-2.4764	0.0133*
B-does the child feel pain / apply pressure while passing stools	Baseline	2.3	0.6	2.0	0.5	2.3	0.4	2.0	0.5	442.00	0.1109	0.9117
	At the end of 12 weeks	2.1	0.5	2.0	0.0	1.5	0.5	1.5	0.3	225.00	3.3191	0.0009*
C-does the child complaints of hard lump like stools	Baseline	2.3	0.5	2.0	0.5	2.1	0.3	2.0	0.0	360.00	1.3232	0.1858
	At the end of 12 weeks	2.1	0.6	2.0	0.1	1.4	0.5	1.0	0.5	186.50	3.8883	0.0001*
D-does the child passes stools after every 2 to 4 days	Baseline	1.3	0.5	1.0	0.5	1.3	0.5	1.0	0.5	450.00	-0.0074	0.9941
	At the end of 12 weeks	1.3	0.6	1.0	0.5	0.7	0.6	1.0	0.0	220.00	3.3930	0.0007*
3. Abdominal pain												

A-does the pain remain continuous throughout the day?	Baseline	0.5	0.5	0.0	0.5	0.5	0.5	0.0	0.5	450.00	-0.0074	0.9941
	At the end of 12 weeks	0.5	0.5	0.0	0.5	0.5	0.5	0.0	0.5	450.00	-0.0074	0.9941
B-is the pain severe enough to effect his/her daily routine activities	Baseline	1.1	0.4	1.0	0.0	1.1	0.4	1.0	0.0	450.00	-0.0074	0.9941
	At the end of 12 weeks	1.0	0.6	1.0	0.0	0.6	0.6	1.0	0.0	279.50	2.5134	0.0120*
C-Does the pain comes in intervals?	Baseline	1.5	0.5	1.5	0.3	1.4	0.5	1.0	0.5	420.00	0.4361	0.6627
	At the end of 12 weeks	1.4	0.5	1.0	0.5	0.7	0.7	1.0	0.0	204.00	3.6296	0.0003*
D-how often is the belly pain associated with vomiting / reflex issues?	Baseline	2.2	0.6	2.0	0.5	1.9	0.4	2.0	0.0	337.00	1.6632	0.0963
	At the end of 12 weeks	1.8	0.6	2.0	0.0	1.2	0.7	1.0	0.5	244.50	3.0308	0.0024*
4. Vomiting/reflex problems												
A- how often did your child vomit / throw up?	Baseline	1.8	0.6	2.0	0.0	1.7	0.7	2.0	0.0	406.00	0.6431	0.5201
	At the end of 12 weeks	1.6	0.7	2.0	0.0	1.1	0.8	1.0	0.0	266.00	2.7129	0.0067*
B-how often did your child nauseated but did not vomit?	Baseline	0.2	0.4	0.0	0.1	0.0	0.0	0.0	0.0	345.00	1.5450	0.1224
	At the end of 12 weeks	0.3	0.4	0.0	0.5	0.0	0.0	0.0	0.0	330.00	1.7667	0.0773
C-how often did your child experience burning sensation	Baseline	1.7	0.7	2.0	0.0	1.6	0.7	2.0	0.0	408.50	0.6062	0.5444
	At the end of 12 weeks	1.5	0.7	1.0	0.5	1.2	0.8	1.0	0.5	364.00	1.2641	0.2062
D-how often did your child experience nausea before vomiting	Baseline	2.2	0.7	2.0	0.5	1.9	0.4	2.0	0.0	320.00	1.9146	0.0555
	At the end of 12 weeks	2.0	0.8	2.0	0.1	1.1	0.6	1.0	0.0	172.00	4.1027	0.0001*
***5.* Bloating**												
A- burp (belch) again and again without vomiting?	Baseline	2.1	0.8	2.0	0.5	2.0	0.8	2.0	0.5	418.50	0.4583	0.6467
	At the end of 12 weeks	2.0	0.8	2.0	0.5	1.3	1.1	1.0	0.5	274.50	2.5873	0.0097*
B- Pass a lot of gas very frequently?	Baseline	2.4	0.6	2.5	0.3	2.5	0.6	3.0	0.0	422.00	-0.4066	0.6843
	At the end of 12 weeks	2.2	0.7	2.0	0.5	0.6	0.8	0.0	0.5	86.50	5.3667	0.0001*
C- develop a swollen belly during the day	Baseline	2.1	0.5	2.0	0.0	1.9	0.3	2.0	0.0	380.00	1.0275	0.3042
	At the end of 12 weeks	1.8	0.6	2.0	0.0	0.8	0.4	1.0	0.0	112.50	4.9824	0.0001*
D- swollen or gulp extra air?	Baseline	0.2	0.4	0.0	0.1	0.2	0.4	0.0	0.1	450.00	-0.0074	0.9941
	At the end of 12 weeks	0.2	0.4	0.0	0.1	0.2	0.4	0.0	0.1	450.00	-0.0074	0.9941

**p<0.05*

The intervention group was found to be a significant predictor of change in scores (p<0.001***). The HMO group was found to decrease the scores by 9.36 as compared to the Inulin Group in post-test. (Table 5).

Discussion

The study population consisted of autistic children aged 4 to 10 years, with a mean age of 5.59±1.28, with gut dysfunction diagnosed using the Rome III criteria for functional gastrointestinal disorders. The study population consisted of 60 children, 66.77% male and 33.33% female). (Table 3) This is an open randomized comparative trial to compare the effects of two different known prebiotics, Human Milk Oligosaccharides (HMO) and Inulin on GI Functions. The establishment of an effective GI microbiota is associated with prebiotics, such as Inulin and HMO. A novel and promising finding of our study is the significant decline in the ROME III Criteria Total Scores in the group treated with HMO (11.6), whereas with inulin (2.24), the total significant decrease was 9.36. (Table 4)

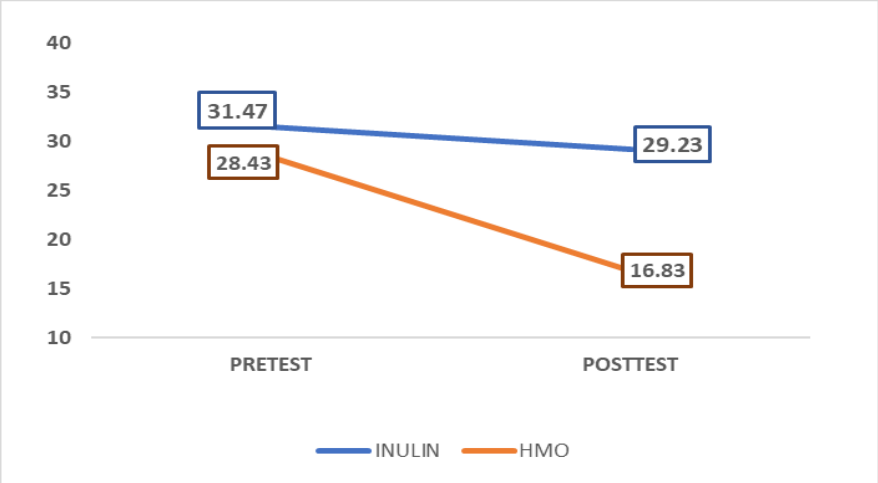

Figure 2: Interaction between HMO and Inulin at Baseline and End

Table 6: Multiple linear regression for determining predictors of change.

Variables	Estimates	p-value
Age		
Reference (≤ 6)	0.156	0.818
(> 6)		
Sex		
Males	0.131	0.847
Females		
Group		
Inulin	9.36	<0.001 ***
HMO		

Change = At Baseline – At end of 12 weeks

The intervention group was found to be a significant predictor of change in scores (p<0.001***). The HMO group was found to decrease the scores by 9.36 as compared to the Inulin Group at end (Table 6)

The primary findings of this study are that HMO has shown significant improvement in treating GI symptoms such as diarrhoea, constipation, abdominal pain, vomiting, and bloating in children with autism

compared to inulin. (Table 5). This was supported by the multi-linear regression model, which showed that HMO was better than inulin in the treatment of GI dysfunction in children with autism, and this effect was independent of other study variables. (Figure 2 & Table 6)

Previous studies have reported an increased incidence of GI symptoms in Autistics Disorders, including constipation, diarrhoea, chronic abdominal pain, nausea, and vomiting. Gut microbiota plays an active role in neurodevelopmental processes, including synaptic pruning. It is well documented that synaptic pruning occurs between the age of 02–10 years of age. Dysregulated synaptic pruning can further contribute to gut dysbiosis [19-21].

To the best of our knowledge, this is the first study to compare the effects of two prebiotics, Inulin and HMO in GI dysfunction in children with autism. Gastrointestinal (GI) microbiota plays a key role in health and disease. It also has a long-term effect on brain development through the gut–brain axis. The Studies have reported that 40 % of children with autistic disorders have GI symptoms, which may be related to gut dysbiosis due to the inflammatory state [22-25]. The numbers of preclinical studies have reported that dysbiosis and alterations of the gut microbiota play a key role in pathogenesis of psychiatric issues in children with autistic spectral disorders [26-27]. Figure 3-The below diagram shows how gut dysbiosis can stimulate the inflammatory cascade in autistic children. Pathogenic bacteria bind to glycan receptors and alter mucosal integrity, thereby causing leaky gut, resulting in poor absorption, gut disturbances, and dysregulated immune and neural functioning [28].

Figure 4 shows how the administration of HMO improves leaky gut symptoms by modification of glycan receptors. HMO's are selectively utilized by beneficial bacteria to promote its growth [29].

Figure 5 shows the mechanism of action of specific strains of Bifidobacterium spp., such as B. longus, B bifidum, and B. breve, which captures, utilizes, and further breaks HMO's by translocation to promoting their growth [30]

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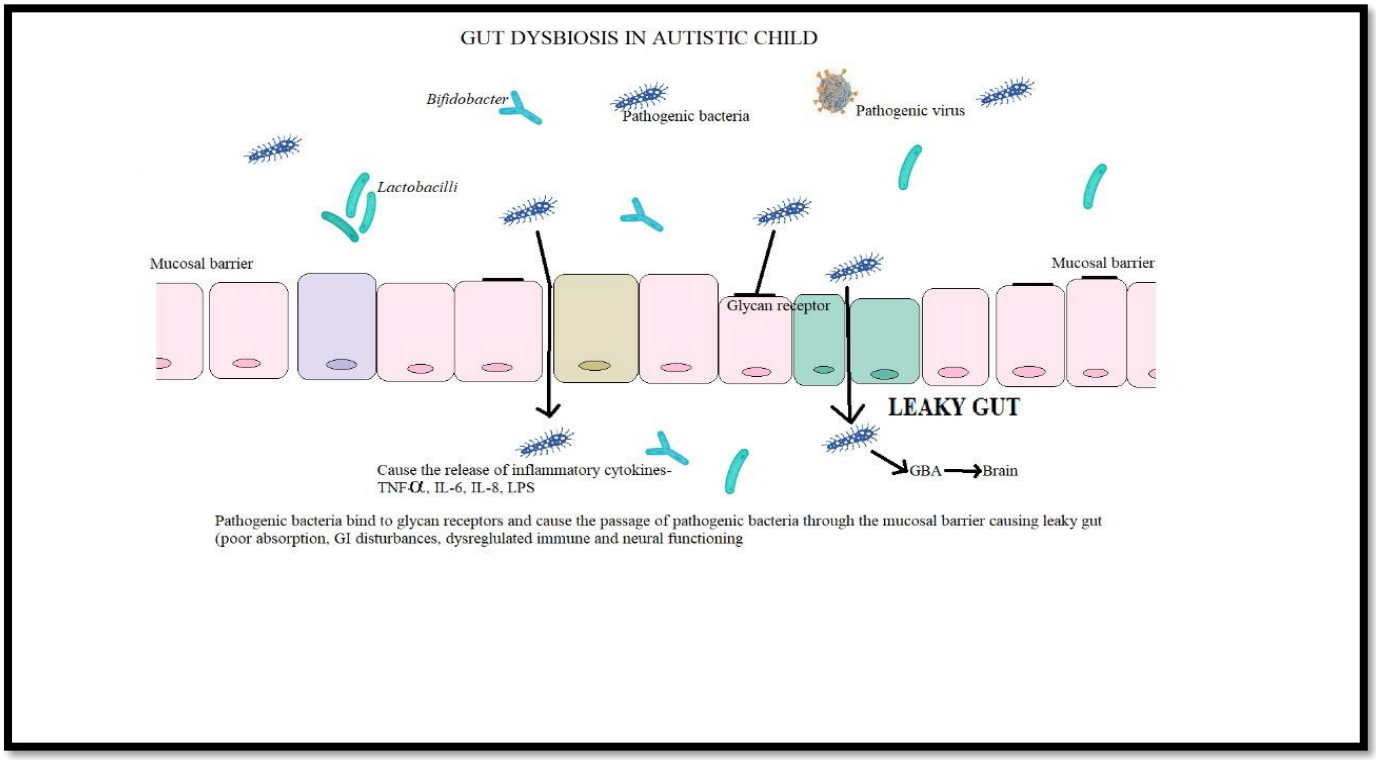

Figure 3: Gut Dysbiosis in Autistic Child

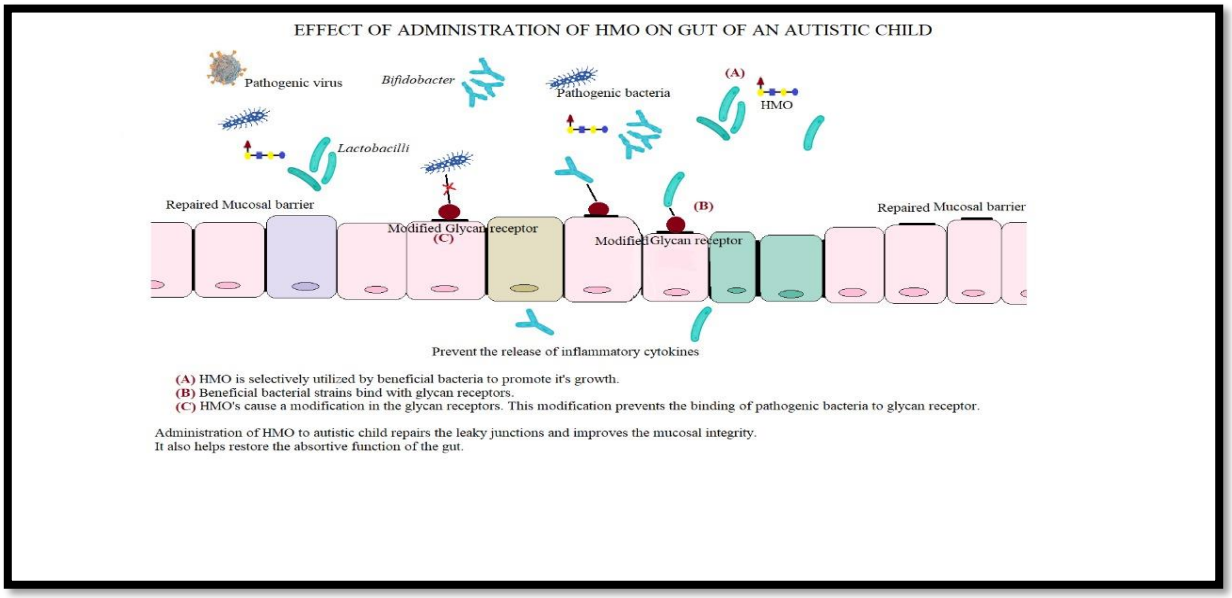

Figure 4: Effect of Administration of HMO on Gut of Autistic Child.

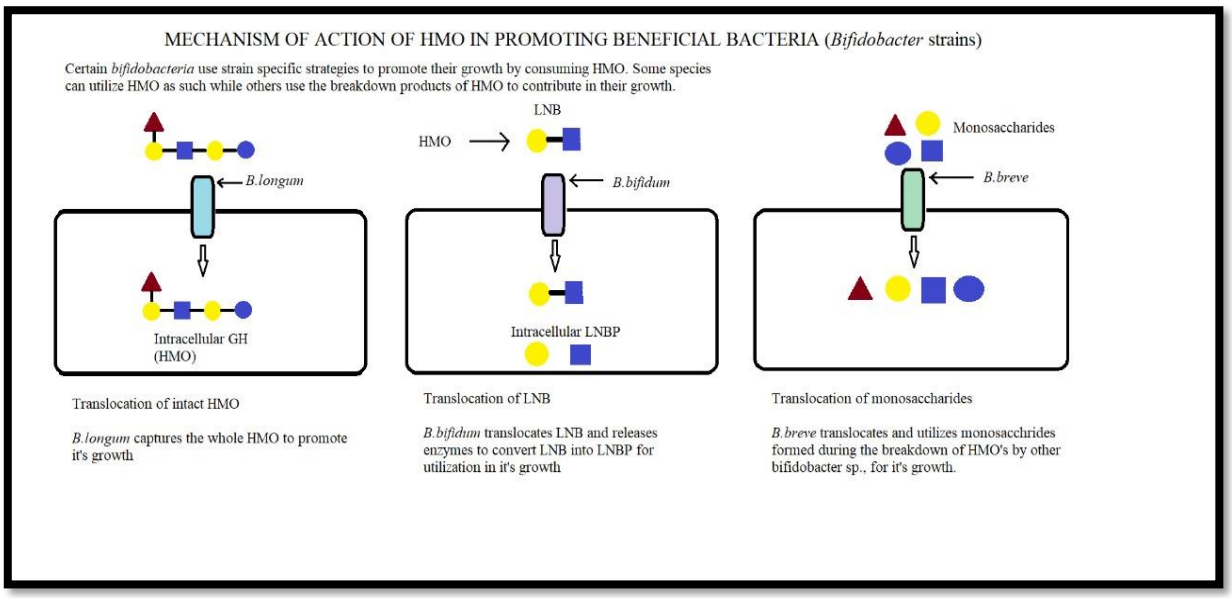

Figure 5: Mechanism of Action of HMO in promoting Gut Bacteria (Adapted from *Sela and Mills, Trends Microbiol,2010) [30].*

In animal studies, there is evidence that prebiotics, such as HMOs, can influence brain activity and cognitive development. This further suggests that diversifying the GI microbiota by dietary means can affect a wide range of diseases. Prebiotics are known to promote the growth of beneficial bacteria, such as Bifidobacteria, in the GI tract, which is associated with numerous beneficial health outcomes. They alleviate the symptoms of autism by affecting the gut-brain axis. However, there are certain advantages and benefits of using HMO over inulin in managing gut microbiota, as they selectively increase the growth of beneficial bacteria and inhibit the growth of non-beneficial bacteria [31-32]. HMO serve as antimicrobial and anti-adhesive agents by preventing the formation of biofilm thereby keeping the potential pathogens in check. (Figure 4 and 5), respectively. They also have direct effects on epithelial cells as well as on immune cells, both locally and systemically in the GI tract [33-34]. Certain bifid bacteria use strain-specific strategies to comprehensively utilize HMOs for growth [35-36].

However, clinical evidence supporting such interactions in humans remains scarce. Although a variety of

mechanisms have been proposed to support interactions within the microbiome gut-brain axis (MGBA), the gut microbiota (GM) primarily communicates with the central nervous system (CNS) via neural, immune-related, endocrine, and metabolic signalling pathways [37-41]. Chemically, the GM and brain communicate with each other using hormones such as corticotrophin-releasing hormone (CRH) in the hypothalamic-pituitary-adrenal (HPA) axis, neurotransmitters such as serotonin (5-HT), dopamine, and γ-aminobutyric acid (GABA), neuropeptides, and short-chain fatty acids (SCFAs) [42-43]. Previous studies have also reported similar findings with the use of different probiotics and prebiotics on autism and have also shown improvement in GI scores [44-45].

Conclusion

Our study concluded; a 12 week prebiotic supplementation resulted in better GI outcomes in children with autism. HMO was found to be more beneficial than inulin for the treatment of GI symptoms in children with autism. These findings could pave the way for further studies on larger subgroups of children with autism, with the aim of improving GI functions and strengthening the gut brain axis.

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Conflict of Interest

The author declares no conflict of interest.

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