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ORIGINAL ARTICLE

Effects of synbiotic supplementation on anthropometric indices and body composition in overweight or obese children and adolescents: a randomized, double-blind, placebo-controlled clinical trial

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Abstract

Background Recently, beneficial effects of probiotics and/or prebiotics on cardio-metabolic risk factors in adults have been shown. However, existing evidence has not been fully established for pediatric age groups. This study aimed to assess the effect of synbiotic on anthropometric indices and body composition in overweight or obese children and adolescents.

Methods This randomized double-blind, placebo-controlled trial was conducted among 60 participants aged 8–18 years with a body mass index (BMI) equal to or higher than the 85th percentile. Participants were randomly divided into two groups that received either a synbiotic capsule containing 6×10^9 colony forming units (CFU) *Lactobacillus coagulans* SC-208, 6×10^9 CFU *Lactobacillus indicus* HU36 and fructooligosaccharide as a prebiotic ($n=30$) or a placebo ($n=30$) twice a day for eight weeks. Anthropometric indices and body composition were measured at baseline and after the intervention.

Results The mean (standard deviation, SD) age was 11.07 (2.00) years and 11.23 (2.37) years for the placebo and synbiotic groups, respectively ($P=0.770$). The waist-height ratio (WHtR) decreased significantly at the end of the intervention in comparison with baseline in the synbiotic group (0.54 ± 0.05 vs. 0.55 ± 0.05, $P=0.05$). No significant changes were demonstrated in other anthropometric indices or body composition between groups.

Conclusions Synbiotic supplementation might be associated with a reduction in WHtR. There were no significant changes in other anthropometric indices or body composition.

Keywords Anthropometry · Body composition · Pediatrics · Synbiotics

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Background

Childhood obesity is a global health concern. It is estimated that the prevalence of overweight in preschool children will increase to 11% worldwide by 2025 [1]. Pediatric obesity is associated with cardiovascular and metabolic diseases [2]. It increases the risk of adult-onset obesity. Obesity or overweight can reduce life expectancy or quality of life [3]. Treatment of obesity is more challenging than its prevention [4].

Several factors, including genetic susceptibility and environmental factors, are associated with obesity. Some modifiable factors, such as lifestyle and diet, are important for national prevention policies. The gut microbiota is a new point of interest that plays a role in the pathophysiology of obesity. It is associated with body weight control, energy homoeostasis,

host energy storage and inflammation [5]. Some lifestyle factors, including lack of exercise, smoking habits and stress, can alter gut microbiota composition. Dietary habits and the composition of nutrients have been suggested as the main geographical factors associated with gut microbiota composition. Some nutrients and bioactive compounds, including probiotics (including yogurts) and prebiotics (fibers and polyphenols), influence the microbiome. Unhealthy dietary patterns, such as Western diets, have been associated with the development of obesity and induce gut dysbiosis [6]. The amount and type of energy source can impact the composition of gut microbiota [7, 8]. Studies have shown reduced levels of *Clostridium perfringens* and *Bacteroidetes* in obese subjects compared to lean subjects. *Bacteroides thetaiotamicron* in association with *Methanobrevibacter smithii* increases adipose tissue accumulation. An imbalanced *Firmicutes/Bacteroidetes* ratio, associated with an increase in the *Actinobacteria phylum* and a decrease in *Verrucomicrobia* in obesity, was confirmed [9]. The findings suggested a dose-dependent association between certain species of bacteria and obesity. In particular, there is a clear relationship between the number of *Lactobacillus reuteri* cells and obesity. Excess weight is associated with a higher number of *L. reuteri* [10].

Human and animal studies have shown that the composition of gut microbiota varies in obese and lean subjects. The major types of bacteria in the body are *Firmicutes* and *Bacteroidetes*. *Firmicutes* is more abundant than *Bacteroidetes* in obese people [7]. Thus, decreasing *Firmicutes* and increasing *Bacteroidetes* will be helpful for obese people.

Nutritional interventions such as probiotics, prebiotics and synbiotics (a mixture of probiotics and prebiotics) can improve the gut microbiota [11]. Synbiotics have the simultaneous properties of probiotics and prebiotics and may influence the survival of probiotics in the gastrointestinal tract [12]. Therefore, a suitable combination of both probiotics and prebiotics in a single product might have a better impact on host health in comparison with the separate activity of probiotics or prebiotics [13]. However, some studies did not show any significant effects of synbiotics on weight and body mass index (BMI) [14, 15].

Different strains of the probiotic family have shown various impacts on cardio-metabolic risk factors, including obesity [16]. A combination of several strains is likely to be more effective than one strain. The present study aimed to determine the potential effects of synbiotic supplementation on anthropometric indices and body composition in overweight or obese children and adolescents.

Methods

Study design

This project was a randomized double-blind placebo-controlled study. It was conducted on 60 overweight or obese children aged between 8 and 18 years with a body mass index (BMI) equal to or higher than the age- and sex-specific 85th percentile according to the World Health Organization percentiles [17]. Use of antibiotics during the previous three months, having any chronic disease, including diabetes, thyroid disorders, cardiovascular diseases, digestive problems, pancreatic and liver diseases, and non-compliance with the intervention regularly were exclusion criteria. Individuals' compliance with the intervention was assessed by counting the number of capsules remaining in each package (compliance = consuming at least 90% of the capsules delivered during the study) and by weekly phone interview. Additionally, those with a daily diet above 4200 Kcal and below 800 Kcal were excluded from the study [18]. Participants were randomly allocated into two groups, synbiotic and placebo. Participants were randomly assigned based on the permutated block randomization method. The random allocation was carried out using a table of random numbers.

The sample size in the current study was determined using a formula for a parallel design randomized controlled trial in which type I and II error rates were considered 5 and 20% (statistical power of 80%), respectively, and the minimum detectable standardized effect size was considered 0.75 [19]. We considered a 33% additional sample size to cover the potential dropout rates. Finally, 40 individuals were included in each group.

Ethical considerations

The study protocol was in accordance with the Declaration of Helsinki and was approved by the research and ethics committee of Isfahan University of Medical Sciences. The trial was registered, and the number of registrations is IRCT20170501033747N2. A written informed consent form was obtained from parents, and oral assent was obtained from their children after the aims and procedures were explained.

Supplement administration

The synbiotic group received two daily capsules containing 12×10^9 colony forming units (CFU) of probiotics (6×10^9 CFU: *Lactobacillus coagulans* SC-208, 6×10^9 CFU *Lactobacillus indicus* HU36). The prebiotic was short-chain fructooligosaccharide (FOS), and each capsule included 38.5 g FOS (7.7% of each capsule).

Those in the placebo group received two 0.5 g capsules containing maltodextrin. Participants consumed two capsules daily with enough water before lunch and dinner. Synbiotic supplements and the placebo were provided by Shiraz

Mehregan Campus Growth Bio products Company, Shiraz, Iran. The manufacturer assigned synbiotic supplement and placebo into A and B codes and packed them in the same boxes in terms of color, shape and size.

They were also advised to store the supplements in a refrigerator to preserve the bacterial load. Additionally, they refrain from consuming fermented products and foods containing probiotics.

Dietary and physical activity assessment

Dietary intake was evaluated by three-day dietary records at the beginning and the end of the study. Dietary data were analyzed by Nutritionist IV software (First Databank, San Bruno, CA, USA). Data entry was performed by a trained dietitian.

Physical activity was assessed by International Physical Activity Questionnaires (IPAQ) [20]. The questions ask about the time of physical activity during the last seven days. Intensity of activity (i.e., vigorous or moderate) and sedentary behaviors such as watching TV were questioned.

Additionally, participants were advised not to change their usual diet and physical activity during the study period.

Anthropometric measurement assessments

Height was measured by a trained nutritionist to the nearest 0.1 cm with a portable stadiometer (SECA, Hamburg, Germany) without shoes. Weight was measured to the nearest 0.1 kg with a balanced portable digital weight scale (SECA, Hamburg, Germany) with light indoor clothing and no shoes. Body mass index (BMI) was calculated as weight (kg)/height^2 (m). Waist circumference (WC) was measured over the unclothed abdomen at the narrowest point between the rib cage and the superior border of the iliac crest using a nonelastic flexible tape to the nearest 0.1 cm.

Hip circumference (HC) was measured at the widest part of the hip at the level of the greater trochanter to the nearest 0.1 cm. Wrist circumference (WrC) was measured to the nearest 0.1 cm on the dominant arm using a tape meter. Neck circumference (NC) was measured with the most prominent portion of the thyroid cartilage taken as a landmark to the nearest 0.1 cm. The waist-height ratio (WHtR), waist-hip ratio (WHR), abdominal volume index (AVI), conicity index (CI), and a body shape index (ABSI) were calculated using the following formulas:

$$\text{WHR}: \ \text{WC (cm)}/\text{HC (cm)}$$

$$\text{WHtR}: \ \text{WC (cm)}/\text{height (cm)}$$

$$\text{AVI}: \left\{2\times \text{WC}^2\left(\text{cm}^2\right) + 0.7\times [\text{WC (cm)} - \text{HC (cm)}]^2\right\}/1000$$

$$\text{CI}: \text{WC (m)}/0.109 \times \frac{\sqrt{\text{Weight (kg)}}}{\sqrt{\text{Height (m)}}}$$

$$\text{ABSI}: \frac{\text{Waist circumference (cm)}}{\text{BMI}^{2/3} \times \text{height}^{\frac{1}{2}}\ \text{(m)}}$$

Body composition analysis

Bioelectrical impedance analysis was performed using an InBody 720 Body Composition Analyzer (BioSpace Co., Ltd., Seoul, Korea). Sex, age, and height were entered directly into the instrument prior to the impedance measurement. Bare feet were placed on the metal plates of the scale, and the participant firmly grasped the hand grips while placing the thumb and fingers in the standard location as indicated in the operation manual. The InBody uses eight points of tactile electrodes (contact at the hands and feet), and it detects the amount of segmental body water. The technique uses multiple frequencies to measure intracellular and extracellular water separately. Thirty impedances are measured in five parts (right arm, left arm, right leg, left leg and trunk) using six frequency bands (1, 5, 50, 250, 500 and 1000 kHz). Frequencies below 50 kHz measure extracellular water, whereas frequencies above 50 kHz measure total body water. The impedances obtained at each frequency are combined to measure intracellular water and extracellular water. After calculating the body water content by the impedance method, the protein mass (muscle) and the mineral mass (bone) are derived from the body water, and the body fat mass is obtained by subtracting these three components from the body weight. It also calculates skeletal muscle mass.

Statistical analysis

Descriptive data were expressed as the mean ± standard deviation (SD) for quantitative variables and number (percentage) for qualitative variables. After assessment of the normal distribution by the Kolmogorov–Smirnov test, within-group changes were compared by the paired *t* test. For comparison of data between the two groups, we used an independent *t* test for data with a normal distribution. The interaction effect of gender and intervention was assessed by analysis of covariance adjusted for baseline values. A *P* value of less than 0.05 was considered statistically significant. We used SPSS for Windows software (version 20; SPSS, Chicago, IL) for statistical analysis.

Results

Among 80 subjects, 7 subjects in the placebo group and 13 in the synbiotic group dropped out. Twelve participants had to take antibiotics due to viral diseases. Five participants did not want to continue taking the drug for personal reasons, and digestive problems occurred in three participants. A total of 60 subjects (32 girls and 28 boys) completed the study and were included in the final analysis (Fig. 1). The mean (SD) age was 11.07 (2.00) years and 11.23 (2.37) years for the placebo and synbiotic groups, respectively ($P=0.770$). Baseline characteristics at the beginning of the study did not differ significantly between the two groups (Table 1). Baseline carbohydrate intake was significantly different between the two groups. However, there were no significant differences in energy and other nutrient intake within and between groups (Table 2).

There were no significant differences between anthropometric values in the placebo and synbiotic groups at baseline ($P>0.05$, Table 3). The mean WHtR was significantly different before and after the intervention in the synbiotic group ($P=0.05$). There were no significant differences between the mean changes in anthropometric indices between the two groups ($P>0.05$, Table 3).

Table 1 Baseline characteristics of participants in the two groups

Variables	Placebo ($n=30$)	Synbiotic ($n=30$)	P value
Age (y)	11.07 ± 2.00	11.23 ± 2.37	0.770
Gender (female)	19 (59.4)	13 (40.6)	0.121
Height (m)	1.46 ± 0.12	1.48 ± 0.14	0.522
Weight (kg)	54.77 ± 16.11	55.02 ± 15.37	0.950
BMI (kg/m^2)	25.30 ± 4.23	24.70 ± 3.27	0.541
Sleep duration (h)	8.00 ± 0.62	7.85 ± 0.56	0.339
Screen time (h)	4.63 ± 0.93	4.51 ± 0.84	0.598
Physical activity (h)	1.65 ± 0.53	1.48 ± 0.66	0.286

Data are shown as mean ± standard deviation or number (percent). *BMI* body mass index

Body composition was measured at baseline and at the end of the intervention. No significant differences were observed between the other anthropometric indices between the two groups. Body composition was assessed at baseline and after the intervention. However, there were no significant changes between and within groups (Table 4). Sex-stratified analysis revealed no significant changes in anthropometric indices or body composition after the intervention in either sex (Table 5).

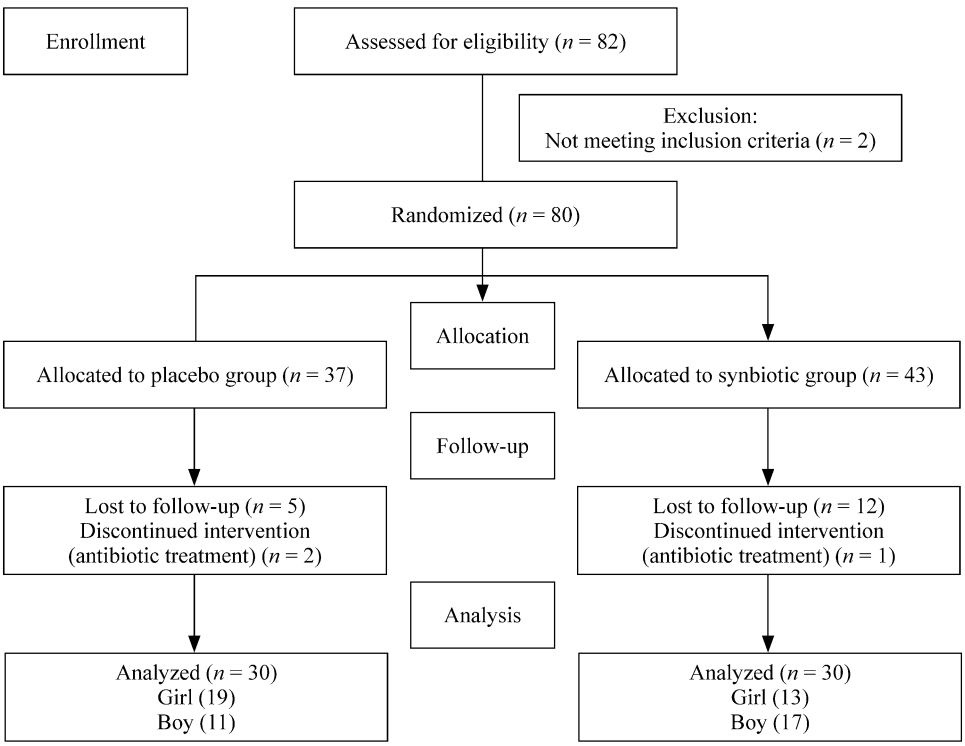

Fig. 1 Study flow diagram

Table 2 Daily dietary intake of participants throughout the study

Variables	Stage	Placebo group ($n=30$)	Synbiotic group ($n=30$)	P^a
Energy (Kcal)	Before	2166.46 ± 444.87	2001.24 ± 289.16	0.093
	After	2125.25 ± 402.08	2018.50 ± 326.64	0.264
	Change	−41.21 ± 193.64	17.26 ± 189.93	0.243
	P^b	0.253	0.622	
Protein (g)	Before	73.86 ± 18.17	68.89 ± 19.15	0.307
	After	71.65 ± 13.34	66.62 ± 15.79	0.188
	Change	−2.21 ± 12.63	−2.26 ± 17.76	0.990
	P^b	0.345	0.491	
Carbohydrate (g)	Before	330.72 ± 79.33	295.75 ± 46.11	0.041
	After	319.76 ± 60.20	295.88 ± 52.87	0.108
	Change	−10.96 ± 48.34	0.13 ± 48.84	0.380
	P^b	0.224	0.988	
Total fat (g)	Before	64.00 ± 15.99	63.13 ± 15.67	0.832
	After	67.66 ± 20.94	66.15 ± 16.72	0.758
	Change	3.66 ± 15.30	3.02 ± 16.00	0.874
	P^b	0.200	0.310	
Saturated fat (g)	Before	16.98 ± 4.76	16.72 ± 5.08	0.837
	After	18.47 ± 6.34	17.36 ± 6.33	0.504
	Change	1.48 ± 6.19	0.65 ± 5.91	0.594
	P^b	0.200	0.555	
Mono unsaturated fat (g)	Before	19.08 ± 7.34	22.33 ± 9.63	0.148
	After	21.41 ± 9.68	22.55 ± 9.73	0.652
	Change	2.33 ± 6.18	0.22 ± 6.23	0.193
	P^b	0.050	0.845	
Poly unsaturated fat (g)	Before	20.85 ± 7.73	17.87 ± 9.43	0.186
	After	21.28 ± 11.32	19.00 ± 9.64	0.403
	Change	0.43 ± 8.14	1.13 ± 7.79	0.736
	P^b	0.773	0.434	
Cholesterol (mg)	Before	223.27 ± 144.73	188.35 ± 121.23	0.315
	After	192.17 ± 84.24	173.62 ± 140.87	0.538
	Change	−31.10 ± 175.48	−14.73 ± 154.99	0.703
	P^b	0.340	0.607	
Linoleic fat (g)	Before	19.77 ± 7.55	16.74 ± 9.37	0.173
	After	20.25 ± 11.12	17.85 ± 9.42	0.372
	Change	0.48 ± 7.95	1.12 ± 7.88	0.756
	P^b	0.744	0.443	
Linolenic fat (g)	Before	0.38 ± 0.34	0.39 ± 0.34	0.925
	After	0.42 ± 0.56	0.43 ± 0.47	0.929
	Change	0.04 ± 0.56	0.05 ± 0.37	0.976
	P^b	0.691	0.516	
Total fiber (g)	Before	18.79 ± 6.90	15.96 ± 5.23	0.079
	After	17.07 ± 4.61	15.62 ± 5.12	0.253
	Change	−1.72 ± 6.48	−0.34 ± 3.89	0.324
	P^b	0.158	0.633	

Data are presented as means ± standard deviations. [a]*P* value resulted from independent *t* test for difference between probiotic and placebo groups based on after intervention and mean changes. [b]*P* value resulted from paired *t* test for difference within groups throughout the study

Table 3 The effect of synbiotic on anthropometric measurements in comparison with placebo

Variables	Placebo ($n=30$)	Synbiotic ($n=30$)	P^a
Weight (kg)			
Before	54.77 ± 16.11	55.02 ± 15.37	0.950
After	54.89 ± 16.52	54.90 ± 15.15	0.998
Change	0.12 ± 2.15	−0.12 ± 1.87	0.644
P^b	0.763	0.723	
Height (m)			
Before	1.46 ± 0.12	1.48 ± 0.14	0.522
After	1.46 ± 0.12	1.48 ± 0.14	0.517
Change	0.0025 ± 0.004	0.002 ± 0.0051	0.784
P^b	0.2	0.6	
BMI (kg/m^2)			
Before	25.30 ± 4.23	24.70 ± 3.27	0.541
After	25.24 ± 4.35	24.58 ± 3.33	0.509
Change	−0.05 ± 0.78	−0.12 ± 0.75	0.747
P^b	0.717	0.400	
Waist circumference (m)			
Before	0.80 ± 0.10	0.80 ± 0.08	0.983
After	0.80 ± 0.10	0.80 ± 0.08	0.922
Change	−0.0003 ± 0.02	−0.0022 ± 0.01	0.599
P^b	0.913	0.214	
Waist-to-hip ratio			
Before	0.87 ± 0.05	0.86 ± 0.06	0.693
After	0.87 ± 0.05	0.84 ± 0.15	0.333
Change	0.0002 ± 0.02	−0.02 ± 0.13	0.315
P^b	0.952	0.319	
WHtR			
Before	0.55 ± 0.06	0.55 ± 0.05	0.580
After	0.55 ± 0.06	0.54 ± 0.05	0.536
Change	−0.0014 ± 0.01	−0.0024 ± 0.01	0.657
P^b	0.446	0.05	
Hip circumference (m)			
Before	0.93 ± 0.11	0.94 ± 0.09	0.811
After	0.93 ± 0.11	0.93 ± 0.09	0.850
Change	−0.0007 ± 0.02	−0.0020 ± 0.01	0.722
P^b	0.827	0.363	
Neck circumference (m)			
Before	0.33 ± 0.03	0.33 ± 0.03	0.903
After	0.33 ± 0.02	0.45 ± 0.65	0.315
Change	−0.0027 ± 0.01	0.12 ± 0.64	0.308
P^b	0.129	0.323	
Wrist circumference (m)			
Before	0.16 ± 0.01	0.16 ± 0.01	1.000
After	0.16 ± 0.01	0.16 ± 0.01	0.620
Change	−0.0008 ± 0.0030	0.0007 ± 0.0022	0.3
P^b	0.134	0.103	
ABSI			
Before	0.08 ± 0.01	0.08 ± 0.01	0.676
After	0.08 ± 0.01	0.08 ± 0.01	0.681
Change	−0.0000 ± 0.0010	−0.0000 ± 0.0011	0.963
P^b	0.985	0.935	
AVI			
Before	2330.61 ± 1842.48	2632.04 ± 2120.18	0.559
After	2331.86 ± 1913.49	2625.16 ± 2158.52	0.580
Change	1.25 ± 584.62	−6.87 ± 289.06	0.946
P^b	0.991	0.897	
CI (g)			
Before	45.20 ± 10.36	44.84 ± 8.62	0.885
After	45.21 ± 10.68	44.64 ± 8.56	0.822
Change	0.01 ± 1.70	−0.20 ± 1.17	0.586
P^b	0.985	0.356	

AVI abdominal volume index, *CI* conicity index, *ABSI* a body shape index, *BMI* body mass index, *WHtR* waist-height ratio. [a]Comparison between group. [b]Comparison within group

Table 4 The effect of synbiotic on body composition in comparison with placebo

Variables	Placebo ($n=30$)	Synbiotic ($n=30$)	P^a
Body fat mass (kg)			
Before	20.98 ± 8.69	21.30 ± 5.99	0.867
After	21.25 ± 9.03	21.31 ± 6.02	0.973
Change	0.27 ± 1.30	0.01 ± 1.43	0.469
P^b	0.264	0.960	
Mineral content (kg)			
Before	2.33 ± 0.78	2.45 ± 0.87	0.596
After	2.36 ± 0.79	2.44 ± 0.87	0.715
Change	0.03 ± 0.08	−0.01 ± 0.07	0.075
P^b	0.045	0.687	
Protein content (kg)			
Before	6.56 ± 2.15	6.81 ± 2.23	0.669
After	6.54 ± 2.12	6.75 ± 2.12	0.702
Change	−0.02 ± 0.25	−0.06 ± 0.32	0.658
P^b	0.617	0.344	
Skeletal muscle mass (kg)			
Before	17.68 ± 6.44	18.50 ± 6.63	0.628
After	17.34 ± 6.96	18.35 ± 6.47	0.559
Change	−0.35 ± 1.75	−0.15 ± 0.67	0.572
P^b	0.290	0.231	
Total body water (L)			
Before	24.40 ± 7.87	24.96 ± 8.38	0.791
After	24.30 ± 7.80	24.83 ± 8.23	0.799
Change	−0.10 ± 0.79	−0.13 ± 0.88	0.890
P^b	0.494	0.427	

[a]Comparison between group. [b]Comparison within group

Table 5 Subgroup analysis based on gender on the effects of synbiotic and placebo consumption on anthropometric measurements and body composition

Variables	Stage	Female ($n=32$)		Male ($n=28$)		*P* for interaction
		Placebo ($n=19$)	Synbiotic ($n=13$)	Placebo ($n=11$)	Synbiotic ($n=17$)	
Weight	Before	51.56 ± 14.41	57.65 ± 13.82	60.30 ± 18.05	53.01 ± 16.59	0.652
	After	51.69 ± 14.97	57.79 ± 14.28	60.42 ± 18.31	52.69 ± 15.85	
	Change	0.12 ± 1.64	0.14 ± 2.04	0.11 ± 2.93	−0.32 ± 1.76	
Height	Before	1.42 ± 0.10	1.48 ± 0.10	1.52 ± 0.14	1.47 ± 0.16	0.968
	After	1.42 ± 0.10	1.49 ± 0.10	1.52 ± 0.14	1.48 ± 0.16	
	Change	0.0026 ± 0.0042	0.0031 ± 0.01	0.0023 ± 0.0041	0.0026 ± 0.0044	
BMI	Before	25.08 ± 4.51	25.80 ± 3.25	25.67 ± 3.89	23.85 ± 3.11	0.816
	After	25.03 ± 4.63	25.75 ± 3.36	25.61 ± 3.99	23.69 ± 3.12	
	Change	−0.05 ± 0.64	−0.05 ± 0.79	−0.06 ± 1.02	−0.16 ± 0.73	
WC	Before	0.79 ± 0.11	0.83 ± 0.08	0.82 ± 0.08	0.79 ± 0.08	0.855
	After	0.79 ± 0.11	0.83 ± 0.08	0.82 ± 0.09	0.78 ± 0.08	
	Change	−0.0000 ± 0.01	−0.0008 ± 0.01	−0.0009 ± 0.02	−0.0032 ± 0.01	
WHR	Before	0.86 ± 0.06	0.86 ± 0.05	0.87 ± 0.02	0.86 ± 0.06	0.141
	After	0.87 ± 0.06	0.81 ± 0.22	0.87 ± 0.04	0.86 ± 0.06	
	Change	0.0010 ± 0.01	−0.06 ± 0.19	−0.0012 ± 0.03	0.0014 ± 0.01	
WHtR	Before	0.56 ± 0.07	0.56 ± 0.04	0.54 ± 0.04	0.54 ± 0.05	0.882
	After	0.56 ± 0.07	0.56 ± 0.04	0.54 ± 0.03	0.53 ± 0.05	
	Change	−0.0011 ± 0.01	−0.0016 ± 0.01	−0.0020 ± 0.01	−0.0030 ± 0.01	
HC	Before	0.92 ± 0.11	0.96 ± 0.10	0.95 ± 0.10	0.92 ± 0.09	0.194
	After	0.92 ± 0.12	0.96 ± 0.10	0.95 ± 0.10	0.91 ± 0.09	
	Change	−0.0011 ± 0.01	0.0023 ± 0.01	−0.0000 ± 0.03	−0.01 ± 0.01	
NC	Before	0.32 ± 0.02	0.34 ± 0.03	0.34 ± 0.03	0.32 ± 0.02	0.592
	After	0.32 ± 0.02	0.61 ± 0.99	0.33 ± 0.03	0.32 ± 0.02	
	Change	−0.00 ± 0.01	0.27 ± 0.97	−0.01 ± 0.01	−0.00 ± 0.00	
Wrist	Before	0.16 ± 0.01	0.16 ± 0.01	0.17 ± 0.01	0.16 ± 0.01	0.300
	After	0.16 ± 0.01	0.16 ± 0.01	0.17 ± 0.01	0.16 ± 0.01	
	Change	−0.00 ± 0.00	0.0012 ± 0.0030	−0.0023 ± 0.0047	0.0003 ± 0.0012	
ABSI	Before	0.08 ± 0.01	0.08 ± 0.0042	0.08 ± 0.0042	0.08 ± 0.01	0.931
	After	0.08 ± 0.01	0.08 ± 0.0044	0.08 ± 0.0044	0.08 ± 0.01	
	Change	0.00002 ± 0.0010	0.000004 ± 0.0009	−0.00004 ± 0.0011	−0.00003 ± 0.0012	
AVI	Before	2281.51 ± 1885.42	2878.60 ± 2313.75	2415.42 ± 1853.00	2443.49 ± 2011.27	0.211
	After	2250.46 ± 1840.96	2988.49 ± 2373.68	2472.45 ± 2117.39	2347.32 ± 2007.43	
	Change	−31.05 ± 227.97	109.89 ± 282.45	57.03 ± 944.56	−96.17 ± 268.44	
CI	Before	43.87 ± 10.74	47.33 ± 8.28	47.49 ± 9.72	42.94 ± 8.62	0.809
	After	43.90 ± 11.08	47.28 ± 8.33	47.46 ± 10.05	42.63 ± 8.42	
	Change	0.03 ± 1.15	−0.05 ± 1.35	−0.03 ± 2.44	−0.31 ± 1.04	
Fat mass	Before	21.42 ± 8.22	23.95 ± 6.78	21.56 ± 8.08	18.40 ± 6.00	0.928
	After	21.55 ± 8.79	23.98 ± 6.99	21.91 ± 7.89	18.50 ± 6.04	
	Change	0.14 ± 1.33	0.03 ± 1.36	0.35 ± 1.96	0.10 ± 0.99	
Mineral body mass	Before	2.11 ± 0.55	2.39 ± 0.74	2.71 ± 0.98	2.49 ± 0.98	0.543
	After	2.14 ± 0.54	2.39 ± 0.76	2.75 ± 1.01	2.48 ± 0.96	
	Change	0.02 ± 0.08	−0.0015 ± 0.08	0.04 ± 0.07	−0.01 ± 0.07	
Protein content (kg)	Before	5.91 ± 1.44	6.64 ± 1.69	7.70 ± 2.72	6.94 ± 2.62	0.736
	After	5.94 ± 1.42	6.62 ± 1.75	7.57 ± 2.74	6.85 ± 2.41	
	Change	0.04 ± 0.18	−0.02 ± 0.27	−0.13 ± 0.33	−0.08 ± 0.36	

Table 5 (continued)

Variables	Stage	Female ($n=32$)		Male ($n=28$)		P for interaction
		Placebo ($n=19$)	Synbiotic ($n=13$)	Placebo ($n=11$)	Synbiotic ($n=17$)	
Skeletal muscle mass (kg)	Before	15.78 ± 4.43	17.98 ± 4.75	20.95 ± 8.14	18.91 ± 7.90	0.518
	After	15.36 ± 5.29	17.98 ± 4.94	20.74 ± 8.36	18.64 ± 7.57	
	Change	−0.42 ± 2.12	−0.00 ± 0.69	−0.21 ± 0.92	−0.26 ± 0.66	
Total body water	Before	22.13 ± 5.52	24.67 ± 5.68	28.33 ± 9.90	25.19 ± 10.14	0.248
	After	22.06 ± 5.34	24.80 ± 5.86	28.18 ± 9.96	24.86 ± 9.85	
	Change	−0.07 ± 0.74	0.13 ± 0.75	−0.15 ± 0.91	−0.33 ± 0.95	

P was resulted from analysis of covariance model including baseline values, group, gender and interaction effect of gender group. *BMI* body mass index, *WC* Waist circumference, *WHR* waist-hip ratio, *WHtR* waist-height ratio, *HC* Hip circumference, *NC* neck circumference, *ABSI* a body shape index, *AVI* abdominal volume index, *CI* conicity index

Discussion

The present study aimed to assess whether a synbiotic combination of *L. coagulans* SC-208 and *L. indicus* HU36 with FOS was effective on anthropometric indices and body composition in overweight or obese children and adolescents. Our results showed that WHtR significantly decreased at the end of the intervention in the synbiotic group in comparison with baseline. No significant changes were demonstrated in other anthropometric indices or body composition between groups.

The results of a recent meta-analysis showed no effect of pro/synbiotic supplementation on BMI, weight, body fat percent and WC among adults with metabolic syndrome [21]. However, another meta-analysis of 23 randomized trials showed that supplementation with a synbiotic can decrease body weight and WC [22]. The reason for the difference in the results may be that the difference in the selected population and the type of intervention.

There are limited human studies that have assessed the effects of probiotics on obesity and anthropometric indices, particularly among pediatric age groups. One month of intervention with synbiotic significantly decreased weight and BMI in obese children and adolescents [23]. Eight weeks of intervention with synbiotic without any lifestyle manipulation reduced BMI *z* score, WC and waist-to-hip ratio [24]. Eight weeks of intervention with *Lactobacillus rhamnosus* in obese children with liver disease showed that *L. rhamnosus* strain GG altered the bacterial composition without any remarkable effect on BMI *z* score or visceral fat [25]. However, 12 weeks of intervention with *Lactobacillus salivarius* (Ls-33) did not show any significant influence on BMI *z* score, WC or body fat in adolescents [26]. Three months of intervention with probiotics [*Bifidobacterium animalis* subsp. *lactis* CECT 8145 (Ba8145)] improved WC, WC/height ratio, conicity index, BMI and visceral fat among adults [27]. Another 12 weeks of intervention with probiotics (*Lactobacillus gasseri* BNR17) showed a slight weight reduction and significant waist and hip circumference changes among obese adults [28], and 12 weeks of intervention with *L. gasseri* SBT2055 showed a beneficial impact on abdominal adiposity and body weight among adults [29]. The differences between our results and other studies could be due to diversity in probiotic strain, composition and dose of supplement, subjects' characteristics, geographical differences, and duration of the intervention.

Animal studies showed that probiotic supplementation with *L. gasseri*, *Lactobacillus curvatus* HY7601 and *Lactobacillus plantarum* KY1032 could decrease abdominal obesity and white adipose tissue size. It may be correlated with a reduction in leptin and adiponectin levels and an increase in the expression of fatty acid oxidation-related genes [30–32]. These findings reveal the effects of probiotics on the modulation of the natural gut microbiota [33]. Evidence has suggested that an imbalance in gut microbiota could contribute to overweight and obesity [22]. Weight loss with a calorie-restricted diet accompanied by increased physical activity has favorable effects on gut microbiota composition [34]. Although the pathogenesis and mechanisms underlying excess adiposity are complex, manipulation of the bacteria in the gastrointestinal system can be considered a potential therapy for overweight and obesity [22].

Initial diversity in the gut microbiota composition in children could be associated with overweight development in adulthood. The impact of probiotics on gut microbiota composition during the first year of life was shown to be a preventive factor for childhood obesity [35]. Intake of *L. rhamnosus* for four weeks before delivery and six months postnatally prevented severe weight gain during the first years of life [36].

The intestinal microbiota increases short-chain fatty acids (SCFAs), including acetate, butyrate and propionate. G-protein coupled receptors 43 and 41 (GPR43 and GPR41) are considered key receptors for SCFA. These two receptors impact the secretion of pancreatic peptide YY (PYY) hormone and leptin and ultimately influence appetite and weight gain [37].

Acetate directly influences the hypothalamus and reduces appetite. Some gut microbiota compounds can suppress the expression of fasting-induced adipose factor (FIAF) protein. This glycoprotein inhibits the production of lipoprotein lipase (LPL) in adipose tissue and the oxidation of fatty acids in both muscle and skeletal muscle [38].

However, the findings are still contradictory, and some mechanisms are controversial. Therefore, further investigation is necessary. The effects of dietary changes and supplements on the human gut microbiota are highly individualized. Findings of the interaction between diet–microbiota and host genetics and epigenetics help us plan new personalized diet approaches and implement new personalized strategies to prevent and decrease the incidence of obesity and other non-communicable diseases [39]. The advantages of the present study are the difference in probiotic strain and pediatric age groups. We assessed several anthropometric indices and body composition.

Intervention during the global pandemic of coronavirus disease 2019 (COVID-19) along with home quarantine and the inability to study enough molecular parameters to reveal molecular mechanisms are limitations of the present study. Our study included children and adolescents, and this age range has a differential impact on gut microbiota. Synbiotic supplements in our study were a combination of two different species, so we could not determine the singular effect and the possible synergistic or antagonistic effects of them. In addition, some studies [24, 28] used the fecal count of gut microbiota to confirm probiotic intake-related changes in intestine flora, but fecal samples were not taken in our study because of financial problems.

In conclusion, synbiotic supplementation might be associated with a reduction in WHtR. Further large-scale studies are required to highlight the importance of the synbiotic on cardio-metabolic risk factors in pediatric age groups.

Author contributions HBM, KR and SJF: conceptualization, writing–review and editing. HBM: formal analysis. AMA: writing–original draft. EMH: review and editing. All authors read and approved the final manuscript.

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Data availability The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Conflict of interest No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

Ethical approval This study was approved by Ethics Committee of Isfahan University of Medical Sciences (Research ethics code: IR.MUI.RESEARCH.REC.1398.449).

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