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ORIGINAL RESEARCH

A Prospective Study on the Association of Mediterranean Diet Adherence and Physical Activity with Inflammatory Bowel Disease in Children

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Video Abstract

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Purpose: This prospective cohort study aims to investigate the potential effects of Mediterranean diet (MD) and physical activity (PA) on the clinical outcomes of pediatric IBD, with the objective of contributing evidence for optimize clinical recommendations.

Patients and Methods: This study included 88 children aged 8–18 years with Crohn's disease (CD) and ulcerative colitis (UC) in Tianjin, China. We advised the participants' parents to implement the MD for their children. We instructed the parents to document their children's PA (in the absence of abdominal symptoms), adherence to MD, and abdominal symptoms on a weekly basis.

Results: Among the 88 children, 66 showed average adherence to the MD, while 22 exhibited good adherence based on established threshold values recorded in the literature. 41 children classified as having low PA and 47 as having high PA. Univariate linear regression analysis indicated that both MD adherence and PA were linked to longer duration of annual abdominal symptoms-free. After adjusting for factors such as age, sex, disease location, disease duration, medication use, and baseline disease activity, good MD adherence remained positively associated with the longer symptom-free duration, while PA did not. In the average MD adherence group, the subgroup with high PA levels experienced a significantly longer annual duration without abdominal symptoms compared to the low PA subgroup. Within the low PA group, those with good MD adherence had a significantly longer symptom-free duration than those with average MD adherence.

Conclusion: MD adherence was independently positive associated with the duration of annual abdominal symptom-free. For children with average MD adherence, high PA level experienced a longer duration of annual abdominal symptom-free.

Keywords: Mediterranean diet, physical activity, inflammatory bowel disease, KIDMED, diet pattern

Introduction

Inflammatory bowel disease (IBD) is a chronic, non-specific inflammatory condition affecting the gastrointestinal tract, primarily encompassing Crohn's disease (CD) and ulcerative colitis (UC). Pediatric patients represent approximately 20–25% of the total IBD population, with a significant annual increase in incidence rates observed among children in emerging industrialized regions of Asia, Africa, and South America. In Asia, the incidence rate ranges from 0.5 to 21.6 per 100,000 individuals per year.[1] In children, the clinical manifestation of IBD is characterized by symptoms such as abdominal pain, diarrhea, and the presence of blood and mucus in stools. As children are in a crucial phase of growth and development, those with IBD face an elevated risk of growth retardation, bone metabolism disorders, delayed puberty, and an increased susceptibility to colon cancer.[2] The poor prognosis and prolonged treatment duration associated with IBD impose a substantial burden on affected children, their families, and society at large. The pathogenesis of IBD remains inadequately understood; however, it is postulated that a multifaceted interaction among genetic predispositions,

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dietary patterns, physical activity (PA), environmental factors, and host immune responses plays a crucial role in the onset of IBD.[3] Within this framework, diet and PA are of particular importance, serving not only as potential precipitants of IBD but also as integral elements in its therapeutic management.[4]

Recent studies have increasingly concentrated on dietary patterns and their role in IBD. The Mediterranean diet (MD) is characterized by a high consumption of vegetables, fruits, whole grains, legumes, and nuts, moderate intake of fish and dairy products, limited consumption of red meat, and the use of virgin olive oil as the primary fat source. Emerging research has demonstrated that adherence to MD patterns is associated with a favorable microbiome composition and reduced inflammation,[5,6] which may be beneficial for children with IBD.[7]

Pediatric patients with IBD frequently exhibit reduced levels of PA. PA has been demonstrated to be advantageous not only for healthy individuals but also for those with autoimmune conditions.[8] The immature immune system and ongoing gut microbiome development in children may amplify the modulatory effects of MD patterns and PA on mucosal healing. Besides, health behaviors established during childhood show greater longitudinal stability. Cohort studies demonstrated that dietary habits and PA established during childhood and adolescence continue into adulthood.[9,10] Targeting MD adherence and PA in children may thus yield sustained benefits. Nowadays, few reports examined the relationship between pediatric IBD and PA, as well as the impact of PA and dietary pattern on the clinical progression of pediatric IBD. This study aims to investigate the potential effects of MD and PA on the clinical outcomes of pediatric IBD, with the objective of contributing evidence for optimize clinical recommendations.

Materials and Methods

Study Population

This prospective cohort study was conducted at Tianjin Children's Hospital, Tianjin, China, within the period of October 2021 to June 2024. The inclusion criteria for participant selection were: (1) aged 8–18 years; (2) diagnosed with UC or CD based on clinical, radiological, and endoscopic criteria; (3) active disease stage, indicated by a pediatric ulcerative colitis activity index (PUCAI) greater than 10 for UC[11] or a pediatric Crohn's disease activity index (PCDAI) greater than 10 for CD;[10] (4) receipt of standardized treatment and follow-up; and (5) acceptance of the invitation to participate in the study. The exclusion criteria included: (1) a history of bowel surgery; (2) use of probiotics or nutritional supplements; and (3) a diagnosis of any other condition that could affect PA or diet.

A total of 106 children, aged 8–18 years and diagnosed with either UC or CD were recruited. 18 participants were excluded: 2 children had undergone bowel surgery, 12 children were using probiotics or nutritional supplements, and 4 children were diagnosed with other diseases that could potentially affect PA or diet (Figure 1).

Data Collection

For the children included in the study, demographic data, including age and gender, were documented. Anthropometric measurements, specifically height and weight, were taken, and height for age Z-score (HAZ) and body mass index for

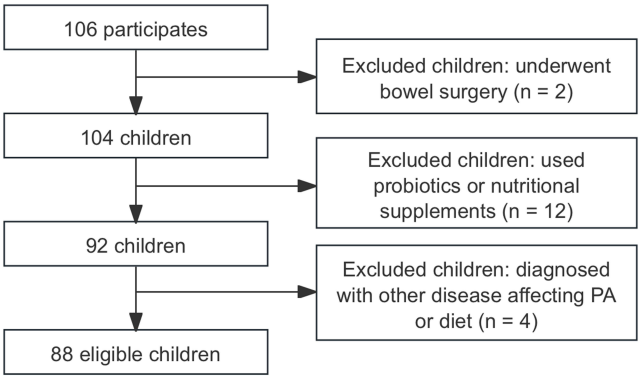

Figure 1 Patient inclusion flowchart.

age Z-score (BAZ) were calculated using the WHO Anthro software (version 3.1.0). HAZ and BAZ have no units. A score of 0 indicates that the measurement is at the median level of the reference population. Positive values indicate that the measurement is greater than the reference median, while negative values indicate that the measurement is less than the reference median. The lower the score, the poorer the nutritional status. Additionally, information regarding the disease, such as age at diagnosis, disease location, disease duration, and medication use, was collected. Disease activity was assessed using established criteria: for CD, the Pediatric Crohn's Disease Activity Index (PCDAI) was used, with scores <10.0 indicating remission, 10.0–27.5 indicating mild activity, 30.0–37.5 indicating moderate activity, and 40.0–100.0 indicating severe activity.[12] For UC, the Pediatric Ulcerative Colitis Activity Index (PUCAI) was employed, with scores <10 indicating remission, 10–34 indicating mild activity, 35–64 indicating moderate activity, and ≥65 indicating severe activity.[11] Blood test parameters, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin (IL) −6, and albumin, as well as fecal calprotectin levels, were assessed.

We provided guidance to the parents of the children, advising them to implement the MD for their children. Specifically, this diet emphasizes the consumption of ample vegetables, fruits, whole grains, legumes, and nuts, while recommending the limitation of red meat intake and the minimization of food processing. In culinary practices, parents were advised to substitute animal fats, which contain saturated fatty acids, with vegetable oils rich in unsaturated fatty acids, such as olive oil, and to avoid various artificial margarines. Additionally, parents were instructed to document their children's PA (in the absence of abdominal symptoms) and adherence to the MD throughout the year, along with any abdominal symptoms (including abdominal pain, bloody stools, stool consistency, 24-hour stool frequency, nocturnal defecation, and activity limitations) on a weekly basis.

After one year, the child underwent a follow-up examination, during which the same blood test parameters and fecal calprotectin levels were re-evaluated. We reassessed HAZ, BAZ, and disease activity. Based on parental records of the child's weekly abdominal symptoms, the duration of annual abdominal symptom-free and the annual recurrence frequency were evaluated.

Assessment of PA

Parents were instructed to use the validated Physical Activity Questionnaire (PAQ) including Physical Activity Questionnaire for Older Children (PAQ-C) and the Physical Activity Questionnaire for Adolescents (PAQ-A) to assess the PA levels of children with IBD weekly during symptom-free periods.[13] The average PAQ score for children during the symptom-free period over the course of a year was calculated. The PAQ-C is administered to children aged 8–14, while the PAQ-A is designed for adolescents aged 15–18. The PAQ-C comprises nine questions addressing the types and frequencies of PA, with each question scored on a scale from 1 to 5. The final score is the mean of the nine items. PAQ-A has the same scoring scheme, except that PAQ-A does not include questions about PA during recess.

Assessment of the Adherence to the MD

The adherence to MD among children with IBD was evaluated using the KIDMED questionnaire.[12] Parents of the participants were instructed to accurately record their children's KIDMED scores on a weekly basis. Subsequently, an annual average KIDMED score was computed. The KIDMED questionnaire comprises 16 items designed to assess children's dietary habits, each requiring a "yes" or "no" response, scored from −1 (indicating a negative connotation) and +1 (indicating a positive connotation). The questionnaire includes four items that reflect a negative connotation to the MD (consumption of fast food, soft drinks, processed breakfast items, and industrial pastries) and twelve items that reflect a positive connotation (consumption of fish, fruits, vegetables, cereals, nuts, pulses, olive oil, fresh food, dairy products, plant-based foods, unprocessed breakfast items, and cooking methods). The total KIDMED scores range from 0 to 12 and are categorized as follows: scores of ≥8 indicate good adherence, scores of 4–7 indicate average adherence, and scores of ≤3 indicate poor adherence to the MD.

Outcomes

The primary outcome assessed was the duration of abdominal symptom-free periods within one year. Secondary outcomes included the frequency of relapses within the same timeframe, changes in HAZ and BAZ after one year

(calculated as ΔHAZ: HAZ at one year minus baseline HAZ; ΔBAZ: BAZ at one year minus baseline BAZ), disease activity at the study endpoint, laboratory indicators at the endpoint (including CRP, ESR, IL-6, albumin, and fecal calprotectin levels). Trained clinical physicians assessed the duration of abdominal symptom-free and the incidence of relapses over the year, based on the parental records of weekly abdominal symptoms in children.

Statistics Analysis

Descriptive statistics were presented as frequencies (proportions) for categorical variables, means ± standard deviations for continuous variables conforming to a normal distribution, and medians (interquartile ranges) for continuous variables not conforming to a normal distribution. To evaluate differences in participants' characteristics across varying levels of MD adherence and PA, categorical variables were analyzed using the chi-square test, continuous variables that followed a normal distribution were assessed using the *t*-test, while those not conforming to normal distribution were evaluated using the Mann–Whitney test. To examine the characteristics associated with the duration of annual abdominal symptom-free, linear regression analysis was employed to investigate the relationship among MD adherence, PA, and the duration of annual abdominal symptom-free.

Statistical significance was determined at a two-sided *P*-value of less than 0.05. All statistical analyses were performed using R software (version 2024.12.1+563).

Results

Characteristics of Participants

The final study cohort comprised 88 children, including 43 males (48.9%), with a average age of 12.8 ± 2.4 years. Within this cohort, 52 participants were diagnosed with UC and 36 with CD. The mean duration of annual abdominal symptom-free was 37.0 ± 11.2 weeks, and the recurrence rate within one year was 1.5 ± 1.1 episodes. Over the year, the average KIDMED score was 6.8 ± 1.5. In the absence of abdominal symptoms within one year, the mean PAQ score was 2.1 ± 0.4. The KIDMED scores were categorized based on established threshold values recorded in the literature.[14] Among the 88 children, 66 demonstrated average adherence to the MD, while 22 exhibited good adherence. The PAQ scores were dichotomized using the median value, resulting in 41 children classified as having low PA and 47 as having high PA.

The results revealed statistically significant differences between the average and good MD adherence groups concerning baseline disease activity, ΔBAZ, the duration of annual abdominal symptom-free, annual recurrence rates, disease activity after one year, laboratory indicators after one year (CRP, calprotectin, and IL-6). Compared to the average MD adherence group, children with good MD adherence experienced less reduction in BAZ, longer symptom-free period, fewer recurrence rates, lower disease activity, and reduced levels of CRP, calprotectin, and IL-6. In comparing the low and high PA groups, significant differences were observed in the duration of annual abdominal symptom-free, CRP, ESR, calprotectin, IL-6, and albumin levels at the endpoint. Children in the high PA group, relative to those in the low PA group, had shorter symptom-free periods, and lower levels of CRP, ESR, calprotectin, and IL-6, but higher albumin levels at the endpoint ($P < 0.05$), as shown in Table 1.

Table 1 Characteristics of Participants

	Overall (N=88)	MD Adherence			PA		
		Average (n=66)	Good (n=22)	P-value	Low (n=41)	High (n=47)	P-value
Baseline							
Age, years	13 (11, 15)	13 (11, 14)	13 (11, 15)	0.738	13 (11, 14)	13 (12, 15)	0.525
Age at diagnosis, years	10.78 (9.40, 12.69)	10.84 (9.31, 12.63)	10.39 (9.63, 12.82)	0.962	10.79 (9.19, 12.33)	10.44 (9.49, 12.73)	0.728
Male, n (%)	43 (48.86)	35 (53.03)	8 (36.36)	0.176	22 (53.66)	21 (44.68)	0.401

(*Continued*)

Table 1 (Continued).

	Overall (N=88)	MD Adherence			PA		
		Average (n=66)	Good (n=22)	P-value	Low (n=41)	High (n=47)	P-value
HAZ	0.31±1.29	0.29±1.35	0.35±1.10	0.853	0.19±1.56	0.4±1.00	0.228
BAZ	−0.75±1.51	−0.65±1.56	−1.05±1.34	0.289	−0.43±1.48	−1.03±1.49	0.059
Medication use							
Medalasine, n (%)	52 (59.09)	42 (63.64)	10 (45.45)	0.328	22 (53.66)	30 (63.83)	0.333
Corticosteroids, n (%)	6 (6.82)	4 (6.06)	2 (9.09)	0.892	3 (7.32)	3 (6.38)	0.862
Biologicals, n (%)	54 (61.36)	37 (56.06)	17 (77.27)	0.373	25 (60.98)	29 (61.70)	0.893
No medication use, n (%)	4 (4.55)	3 (4.55)	1 (4.55)	0.741	2 (4.88)	2 (4.26)	0.889
Disease							
UC, n (%)	52 (59.09)	41 (62.12)	11 (50.00)	0.317	22 (53.66)	30 (85.71)	0.333
CD, n (%)	36 (40.91)	25 (37.88)	11 (50.00)		19 (46.34)	17 (48.57)	
Disease activity							
Mild, n (%)	31 (35.23)	28 (42.42)	3 (13.64)	<0.001	13 (31.71)	18 (38.30)	0.344
Moderate, n (%)	43 (48.86)	24 (36.36)	19 (86.36)		19 (46.34)	24 (51.06)	
Severe, n (%)	14 (15.91)	14 (21.21)	0 (0.00)		9 (21.95)	5 (10.64)	
Disease Duration, years	1.25 (0.65, 2.31)	1.25 (0.66, 2.38)	1.25 (0.52, 1.89)	0.877	1.21 (0.65, 2.15)	1.28 (0.64, 2.46)	0.854
Disease Location							
UC:				0.213			0.581
E1, n (%)	0 (0.00)	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
E2, n (%)	12 (13.64)	8 (12.12)	4 (18.18)		4 (9.76)	8 (17.02)	
E3, n (%)	18 (20.45)	17 (25.76)	1 (4.55)		8 (19.51)	9 (19.15)	
E4, n (%)	22 (25.00)	16 (24.24)	6 (27.27)		10 (24.39)	13 (27.66)	
CD:							
L1, n (%)	0 (0.00)	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
L2, n (%)	11 (12.50)	7 (10.61)	4 (18.18)		7 (17.07)	4 (8.51)	
L3, n (%)	18 (20.45)	12 (18.18)	6 (27.27)		7 (17.07)	11 (23.4)	
L4a, n (%)	3 (3.41)	3 (4.55)	0 (0.00)		2 (4.88)	1 (2.13)	
L4b, n (%)	4 (4.55)	3 (4.55)	1 (4.55)		3 (7.32)	1 (2.13)	
Laboratory indicators							
CRP, mg/L	38.80 (14.10, 58.61)	36.73 (12.60, 55.03)	48.65 (34.95, 59.68)	0.088	45.60 (17.80, 59.81)	35.39 (12.55, 50.01)	0.147
ESR, mm/h	21.00 (15.00, 29.00)	20.00 (14.00, 29.75)	26.00 (19.25, 28.75)	0.332	21.00 (16.00, 30.00)	21.00 (14.5., 29.00)	0.479
Calprotectin, mg/L	230.56 (152.16, 349.76)	224.45 (148.35, 527.38)	249.69 (178.43, 283.47)	0.900	227.16 (152.44, 547.49)	233.96 (148.39, 287.21)	0.268
IL-6, pg/mL	32.18 (22.35, 50.71)	29.14 (17.72, 48.81)	37.65 (34.09, 53.11)	0.076	31.20 (23.42, 89.48)	34.05 (17.95, 48.71)	0.464
Albumin, g/L	40.86±4.41	41.02±4.28	40.41±4.86	0.582	41.04±4.45	40.71±4.41	0.724

(*Continued*)

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Table 1 (Continued).

	Overall (N=88)	MD Adherence			PA		
		Average (n=66)	Good (n=22)	P-value	Low (n=41)	High (n=47)	P-value
One year later							
ΔHAZ	−0.61 (−1.59, 0.26)	−0.68 (−1.74, 0.26)	−0.55 (−1.16, 0.17)	0.298	−0.44 (−1.33, 0.60)	−0.61 (−1.73, −0.07)	0.255
ΔBAZ	−0.7±1.37	−0.71±1.43	−0.67±1.21	<0.001	−0.43±1.40	−0.93±1.32	0.131
Duration of annual abdominal symptom-free, weeks	39.00 (31.50, 47.00)	36.50 (25.00, 44.50)	45.00 (39.25, 48.00)	0.004	36.00 (24.00, 43.00)	41.00 (33.50, 48.00)	0.021
Annual recurrence count	2 (1, 2)	2 (1, 3)	1 (0, 2)	0.018	2 (1, 3)	1 (0.5, 2)	0.083
Disease activity							
None, n (%)	42 (47.73)	26 (39.39)	16 (72.73)	0.003	14 (34.15)	18 (38.30)	0.119
Mild, n (%)	28 (31.82)	22 (33.33)	1 (4.55)		16 (39.02)	12 (25.53)	
Moderate, n (%)	26 (29.55)	16 (24.24)	0 (0.00)		10 (24.39)	6 (12.77)	
Severe, n (%)	2 (2.27)	2 (3.03)	0 (0.00)		1 (2.44)	1 (2.13)	
Laboratory indicators							
CRP, mg/L	3.45 (1.00, 14.30)	6.40 (1.00, 18.40)	1.00 (1.00, 3.20)	0.001	8.00 (2.00, 16.90)	1.00 (1.00, 9.75)	0.016
ESR, mm/h	12.50 (8.00, 18.00)	13.50 (8.00, 20.75)	11.00 (6.25, 15.75)	0.079	16.00 (10.00, 22.00)	11.00 (7.50, 16.00)	0.037
Calprotectin, mg/L	101.22 (63.50, 247.17)	159.38 (76.39, 391.64)	62.11 (31.43, 76.48)	<0.001	165.35 (81.38, 401.91)	75.81 (41.05, 189.04)	0.004
IL-6, pg/mL	5.65 (2.51, 13.93)	9.59 (2.93, 16.13)	3.22 (1.75, 4.83)	<0.001	9.10 (3.39, 16.75)	4.69 (2.08, 11.20)	0.020
Albumin, g/L	43.48±4.00	43.12±4.23	44.55±3.02	0.149	42.25±4.47	44.55±3.22	0.003

Abbreviations: BAZ, body mass index for age Z-score; CD, Crohn's disease; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HAZ, height for age Z-score; IL, interleukin; MD, Mediterranean diet; PA, physical activity; UC, ulcerative colitis.

Correlation Between Mean KIDMED Score, Mean PAQ Score, and the Duration of Annual Abdominal Symptom-Free

The correlation between the mean KIDMED score and the duration of annual abdominal symptom-free is illustrated in Figure 2, while the correlation between the mean PAQ score and the duration of annual abdominal symptom-free is depicted in Figure 3. A prolonged annual abdominal symptom-free period was significantly correlated with higher mean KIDMED scores ($r = 0.529$, $P < 0.001$) and higher mean PAQ scores ($r = 0.337$, $P < 0.001$).

Association Among MD Adherence, PA, and Duration of Annual Abdominal Symptom-Free

The association among MD adherence, PA, and the duration of annual abdominal symptom-free is presented in Table 2. The results of simple linear regression analysis indicated that, compared to children with average adherence, those with good adherence experienced a longer period without abdominal symptoms annually (β: 8.364, 95% CI: 3.171, 13.556, P<0.005). Additionally, higher KIDMED scores were associated with an extended period without abdominal symptoms per year (β: 3.868, 95% CI: 2.537, 5.199, P<0.001). After adjusting for confounding factors such as age, sex, disease location, disease duration, medication use, and baseline disease activity, good adherence and higher KIDMED scores remained significantly associated with a longer period of no abdominal symptoms annually.

The findings from the univariate linear regression analysis indicated that, in comparison to children with low PA, those with high PA experienced a longer duration without abdominal symptoms annually (β: 5.349, 95% CI: 0.721, 9.978, P<0.05). Furthermore, elevated scores on the PAQ were correlated with an extended period free from abdominal symptoms each year (β: 9.532, 95% CI: 3.827, 15.236, P<0.005). Upon adjusting for potential confounders, including

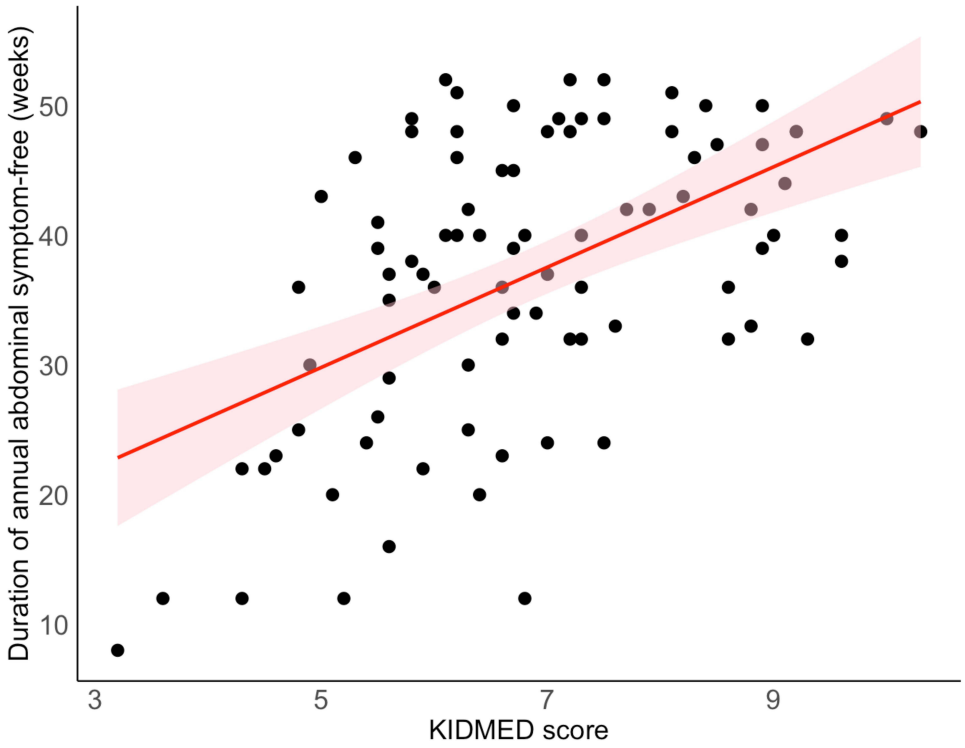

Figure 2 Scatter plots and linear trend line of duration of annual abdominal symptom-free in association with mean KIDMED score.

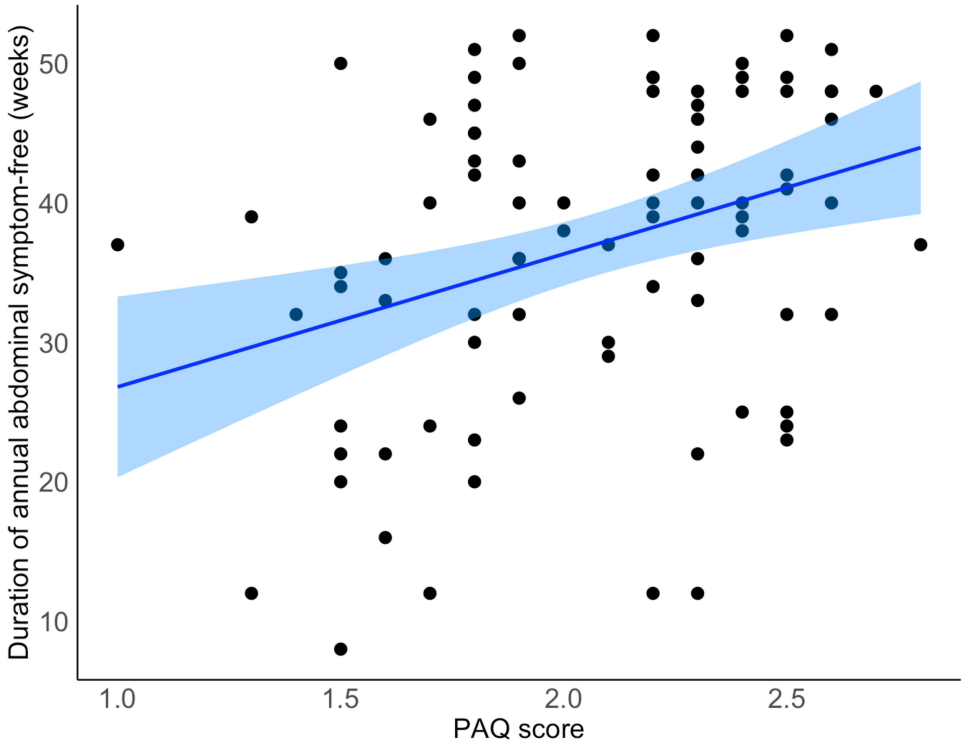

Figure 3 Scatter plots and linear trend line of duration of annual abdominal symptom-free in association with mean PAQ score.

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Table 2 Association Among MD Adherence, PA and the Duration of Annual Abdominal Symptom-Free

Variables	Crude		Model 1		Model 2		Model 3	
	β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
MD adherence								
Average	Reference	–	Reference	–	Reference	–	Reference	–
Good	8.364 (3.171, 13.556)	0.002	7.784 (2.589, 12.979)	0.004	6.277 (0.805, 11.748)	0.025	8.139 (3.63, 12.648)	0.001
KIDMED score (Continuous Variable)	3.868 (2.537, 5.199)	<0.001	3.470 (2.109, 4.832)	<0.001	3.171 (1.722, 4.62)	<0.001	3.358 (2.21, 4.507)	<0.001
PA								
Low	Reference	–	Reference	–	Reference	–	Reference	–
High	5.349 (0.721, 9.978)	0.024	4.759 (0.272, 9.246)	0.038	4.596 (−0.045, 9.237)	0.052	2.775 (−0.985, 6.535)	0.146
PAQ score (Continuous Variable)	9.532 (3.827, 15.236)	0.001	6.473 (1.135, 11.811)	0.018	6.073 (0.544, 11.603)	0.032	2.588 (−1.882, 7.058)	0.252

Notes: Crude: not adjusted for any factors. Model 1: adjusted for age, sex. Model 2: adjusted for age, sex, disease location, disease duration. Model 3: adjusted for age, sex, disease location, disease duration, medication use, disease activity at baseline.
Abbreviations: MD, Mediterranean diet; PA, physical activity; PAQ, physical activity questionnaire.

age, sex, and disease location, the association between PAQ scores and the duration without abdominal symptoms remained significant (β: 6.073, 95% CI: 0.544, 11.603, P<0.05). However, when medication use and baseline disease activity were incorporated into the adjustments, the association between PAQ scores and symptom-free duration was no longer significant.

Subgroup Analysis Stratified by Different MD Adherence and PA's Duration of Annual Abdominal Symptom-Free

Mann–Whitney tests were performed separately for each category of MD adherence and PA. The results, depicted in Figure 4, reveal that among children with average MD adherence, the high PA subgroup had a significantly longer symptom-free period compared to the low PA subgroup (P = 0.021). Conversely, among children with good MD adherence, no significant difference was observed in the symptom-free duration between the low and high PA subgroups (P = 0.807).

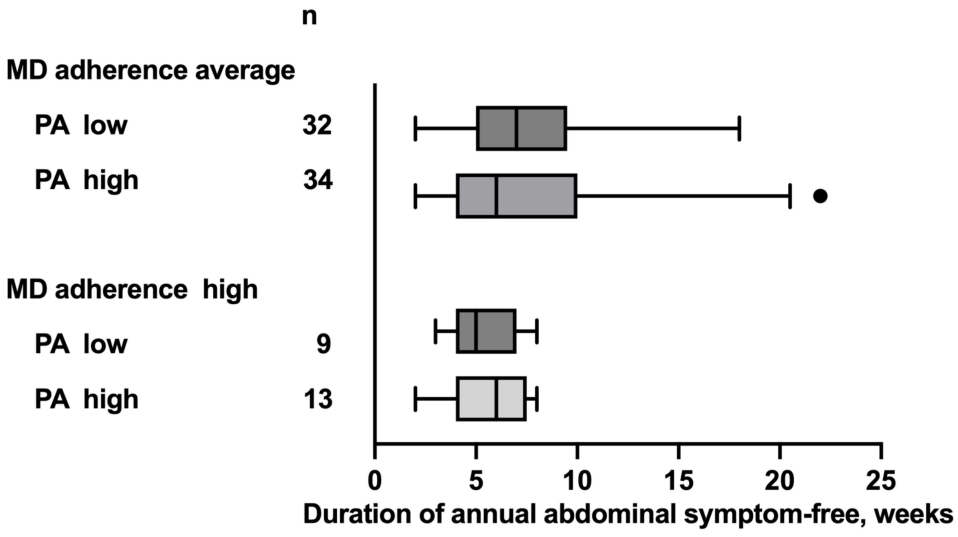

Figure 4 Subgroup analysis stratified by different MD adherence and PA's duration of annual abdominal symptom-free.

In the group with low PA, individuals with good adherence to the MD exhibited a significantly longer duration without abdominal symptoms compared to those with average MD adherence (P = 0.012). Conversely, in the high PA group, no statistically significant difference was observed in the duration without abdominal symptoms between the good and average MD adherence subgroups (P = 0.137).

The black vertical lines indicate the median. The left and the right borders of the box mark the first and the third quartiles. The error bars indicate the 5th and 95th percentiles. The black solid circle indicates the individual whose values were outside the 5th or 95th percentiles.

Discussion

IBD encompasses a group of disorders characterized by chronic inflammation of the intestinal tract, with CD and UC being the primary conditions. Despite differences in their pathological mechanisms and clinical presentations, both diseases involve persistent inflammation of the intestinal mucosa, leading to symptoms such as abdominal pain, diarrhea, and bloody stools. Malnutrition and sarcopenia are prevalent among IBD patients and frequently co-occur, adversely affecting quality of life.[15] Research indicates a positive correlation between insufficient lean body mass and increased disease activity.[16] The symptoms of IBD in pediatric populations may be more severe compared to adults, with children exhibiting a higher susceptibility to extraintestinal manifestations that significantly affect their quality of life and psychological development.[17] Lifestyle factors, particularly diet and PA, may influence the onset and progression of IBD.[18]

Our study identified a positive correlation between adherence to the MD, as defined by the KIDMED score, and the duration of symptom-free periods annually. The KIDMED score, originally developed by Serra-Majem et al, assesses the adherence of children and adolescents to the MD.[19] Recently, López-Gajardo update the questionnaire,[14] and its validity for research applications among children and adolescents has been established.[20–24] A randomized controlled trial demonstrated that children with IBD who achieved a KIDMED score of 8 exhibited significantly lower disease activity scores (PCDAI and PUCAI) and reduced levels of inflammatory markers (CRP, calprotectin, TNF-α, IL-17, IL-12, and IL-13) compared to those with KIDMED scores of 7 or lower,[7] aligning with our findings.

Several mechanisms may underlie the beneficial effects of the MD in managing IBD. The MD is rich in anti-inflammatory and antioxidant compounds, including minerals, vitamins, omega-3 fatty acids, and polyphenols. Additionally, the MD provides a substantial amount of prebiotics, which, upon fermentation in the intestinal tract, are converted into short-chain fatty acids (SCFAs). These SCFAs are thought to play a crucial role in maintaining intestinal flora balance. Research by Haskey et al demonstrated that individuals adhering to the MD exhibited elevated levels of total fecal SCFAs, acetic acid, and butyric acid. Moreover, the MD was associated with changes in microbial species that are protective against colitis, such as *Alistipes finegoldii* and *Flavonifractor plautii*, and with the production of SCFAs by *Ruminococcus bromii*.[5] Similarly, Williams reported that a diet resembling the MD was significantly correlated with a specific microbial composition, characterized by an increased presence of fiber-degrading bacteria like *Ruminococcus* and *Faecalibacterium*.[6] These microbiotas are capable of modulating the host's immune response, enhancing the integrity of the intestinal mucosal barrier, and reducing the translocation of inflammatory mediators, thereby mitigating intestinal inflammation.[25–27]

In this study, the outcomes of univariate analysis and linear regression, adjusted for age and gender, indicated that higher levels of PA were associated with an extended duration without abdominal symptoms. Upon incorporating disease location and disease duration into the regression model, the continuous variable of the PAQ score maintained a positive correlation with the duration without abdominal symptoms. Nevertheless, this association was not observed after adjusting for medication use and baseline disease activity. Recent studies have suggested that PA exerts anti-inflammatory effects on certain autoimmune diseases.[8,28] The existing literature definitively indicates that PA increases the risk of IBD. A Mendelian randomization study, which analyzed 458,109 participants, identified PA as a significant predictor of the development of CD and UC.[29] Furthermore, a meta-analysis suggests that PA is inversely associated with the risk of developing IBD, with a more pronounced effect observed in CD compared to UC.[30]

The relationship between PA and symptom relief in IBD remains inconclusive. Some studies have demonstrated an association between PA and symptom alleviation in IBD. For instance, a study with a small sample size indicated that an

8-week moderate-intensity exercise intervention led to reductions in ESR, CRP, and platelet count in children with IBD.[31] Additionally, a cross-sectional study found that IBD patients with low levels of PA reported the poorest health-related quality of life and highest disease activity, including symptoms such as depression, pain interference, fatigue, sleep disorders, social dissatisfaction, and increased CD's disease activity, compared to those in moderate and high PA groups.[32] Conversely, some studies have not observed a reduction in inflammatory markers in IBD patients due to PA, yet they have reported other potential benefits. For example, a prospective randomized controlled trial revealed that a 10-week moderate-intensity exercise regimen improved the quality of life for IBD patients, although it did not result in changes in CRP levels, fecal calprotectin, or disease activity index.[33]

Cronin et al found that moderate-intensity exercise increased muscle tissue quality, but there were no significant changes in disease activity index and pro-inflammatory cytokines (IL-8, IL-10, IL-6).[34] Mila et al observed an increase in lean mass, bone density, aerobic fitness, and vigorous PA levels in IBD children, but no change in inflammation or muscle strength.[35] Vanhelst et al discovered that PA improved the bone health of children with IBD.[36]

Several studies have reported that 45% of patients with IBD reduce their PA following diagnosis.[37] In the present study, the PAQ scores of children were assessed in the absence of abdominal symptoms. The findings indicated that the average PAQ scores among participants ranged from 2.8 to 1.0, with a median score of 2.15, which is considered relatively low on the PAQ scale of 0–5. This suggests that even in the absence of abdominal symptoms, children engage in PA infrequently. Previous research has demonstrated that moderate-intensity PA can be beneficial for managing intestinal inflammation and IBD.[31,33] Additionally, some studies have identified a positive correlation between increased moderate-to-vigorous PA and enhanced quality of life in IBD patients.[38] Whereas, an animal study demonstrated that repetitive vigorous exercise can trigger systemic inflammatory responses and multi-organ damage in rats, with intestinal manifestations such as mucosal shedding and necrosis.[39] Some researchers argue that intense PA may not be feasible or acceptable for patients with IBD because it could exacerbate intestinal symptoms, worsen existing fatigue, or lead to uncontrolled bowel movements.[40] This suggests that further investigation is needed to understand the relationship between IBD and PA, as well as to determine the appropriate intensity of exercise for IBD patients.

Due to factors such as inflammatory depletion, poor nutrient absorption, and vitamin D deficiency, individuals with IBD frequently experience sarcopenia.[41] Liao et al reported a sarcopenia prevalence of 25.2% among IBD patients and found that low muscle mass at the initiation of anti-tumor necrosis factor treatment was associated with early treatment failure.[15]

Both diet and PA influence the enhancement of muscle mass. Consequently, we investigated the combined impact of dietary patterns and PA on the duration of symptom-free periods in the abdomen. This investigation is instrumental in determining whether the MD and PA might contribute to the progression of IBD through mechanisms related to muscle mass. Previous research has involved a 12-week intervention focusing on a healthy diet and PA in children with IBD. With drug treatments held constant, the intervention group exhibited a significant reduction in disease activity index and fecal calprotectin levels, alongside an improvement in quality of life scores, compared to the control group.[42] Furthermore, some studies have demonstrated that the combined additive effect of low adherence to the MD and low PA on all-cause mortality surpasses the impact of each risk factor individually.[43] Our study identified that at low levels of PA, an increase in adherence to the MD was correlated with a prolonged period without abdominal symptoms. Conversely, when MD adherence was at an average level, an increase in PA was associated with an extended duration free from abdominal symptoms. These findings imply that in situations where children are unable to maintain high levels of MD adherence or PA, enhancing another factor may be beneficial for alleviating abdominal symptoms.

While our findings highlight the beneficial association between MD adherence, PA, and prolonged annual symptom-free duration in pediatric IBD, caution is warranted when extrapolating these conclusions to adult populations due to fundamental pathophysiological and behavioral differences. The developing gut microbiome in children exhibits greater modifiability by dietary interventions compared to the relatively stable adult microbiome. Prospective studies comparing parallel pediatric/adult cohorts are needed to validate these findings across age spectra.

This study has several limitations. The sample size was relatively small, and subgroup analyses for children with CD and UC were not conducted, limiting the understanding of disease-specific effects. External validation was not performed, restricting the generalizability of the findings to other settings. Furthermore, despite parental training on

the KIDMED and PAQ questionnaires at baseline and the implementation of monthly follow-ups, assessment errors were still observed. Additionally, no mechanistic research was conducted to elucidate the underlying pathways.

Future research should focus on multi-center studies with large sample sizes to validate our findings and more objectively assess MD adherence and PA levels. Additionally, it is imperative to investigate the underlying mechanisms through which MD and PA influence IBD.

Conclusion

The univariate linear regression analysis indicated that both MD adherence and PA were correlated with the duration of annual abdominal symptoms-free. Even after adjusting for variables such as age, sex, disease location, disease duration, medication use, and baseline disease activity, good adherence to the MD remained positively associated with the annual symptom-free duration. However, PA did not demonstrate a significant association with this outcome. Within the group with average MD adherence, the subgroup with high PA levels experienced a significantly longer annual duration without abdominal symptoms compared to the low PA subgroup. Conversely, within the low PA group, those with good MD adherence had a significantly longer symptom-free duration than those with average MD adherence. These findings could inform the development of dietary and exercise interventions for pediatric IBD patients.

Abbreviations

BAZ, body mass index for age Z-score; CD, Crohn's disease; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HAZ, height for age Z-score; IBD, inflammatory bowel disease; IL, interleukin; MD, Mediterranean diet; PA, physical activity; PAQ, physical activity questionnaire; PAQ-A, physical activity questionnaire for adolescents; PAQ-C, physical activity questionnaire for older children; PCDAI, pediatric Crohn's disease activity index; PUCAI, pediatric ulcerative colitis activity index; SCFAs, short-chain fatty acids; UC, ulcerative colitis.

Data Sharing Statement

The data that support this study are not openly available due to the ongoing follow-up of the cohort, and are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The study was conducted in compliance with the ethical principles outlined in the "Declaration of Helsinki" and received approval from the Ethics Committee of Tianjin Children's Hospital (Approval No.: L2021-010). Informed consent was obtained from the parents or legal guardians of all pediatric participants included in this study. In addition to parental consent, assent was obtained from children who were capable of understanding the study. The study was explained to the children in an age-appropriate manner, and their willingness to participate was confirmed.

Consent for Publication

All participants gave consent for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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