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RESEARCH ARTICLE

Association between the dietary inflammatory index and spexin levels, metabolic syndrome, and inflammatory biomarkers in children with obesity

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Abstract

Background Chronic low-grade diet-related inflammation has been indicated to affect obesity and metabolic syndrome (MetS). The current study was designed to explore the Dietary Inflammatory Index (DII) in children and its relationship with spexin levels, appetite, and various cardiometabolic factors, including MetS, obesity, insulin resistance, and specific inflammatory biomarkers.

Methods This study included 90 obese adolescents and 90 normal-weight adolescents for overall analysis. A subset of 90 participants (45 obese and 45 normal-weight) provided blood samples for biochemical assays. Dietary intake was assessed using a validated 168-item semi-quantitative food frequency questionnaire, from which the DII score was calculated. Multivariable logistic regression models were employed to evaluate the association between the DII score and cardiometabolic risk factors.

Results The children's mean DII score was −1.25 (±1.01). Higher DII scores (indicating a more pro-inflammatory diet) were significantly associated with increased odds of obesity across all adjusted models (OR: 2.03, 95% CI: 1.10–3.75). A significant positive correlation was found between DII scores and high-sensitivity C-reactive protein levels ($r = 0.30$, $P = 0.005$). In crude analysis, the most anti-inflammatory diet was associated with higher spexin and interleukin-10 levels and a lower appetite score; however, these associations were no longer significant after adjustment for confounders. No significant associations were found between DII and metabolic syndrome or its components.

Conclusion These findings indicate that the influence of the DII on obesity may be primarily mediated through spexin levels, inflammatory markers, and appetite regulation, rather than through direct effects on MetS components.

Keywords Dietary inflammatory index · Spexin · Metabolic syndrome · Obesity · Insulin resistance

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Abbreviations

BMI	Body mass index
CVD	Cardiovascular disease
DII	Dietary inflammatory index
FFQ	Food frequency questionnaire
HDL-C	High-density lipoprotein cholesterol
hs-CRP	High-sensitivity C-reactive protein
IL	Interleukin
LDL-C	Low-density lipoproteins cholesterol
MetS	Metabolic syndrome
FBG	Fasting blood glucose
HOMA-IR	The homeostatic model assessment of insulin resistance
TG	Triglyceride
TNF-α	Tumor necrosis factor-α
WC	Waist circumference
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
MAQ	Modifiable activity questionnaire
CDC	Charts of centers for disease control and prevention
OR	Odds Ratio
CI	Confidence interval

Introduction

Childhood obesity has emerged as a critical public health challenge due to its strong association with chronic low-grade inflammation [1], which serves as the fundamental pathological process underlying numerous non-communicable diseases [2].

Furthermore, obesity in childhood often persists into adulthood, increasing the risk of insulin resistance, hypertension, dyslipidemia, and impaired glucose metabolism [3]. The global obesity epidemic stems largely from environmental and behavioral changes [4], with diet playing a crucial role in promoting an inflammatory state [5]. Unhealthy dietary patterns in childhood tend to persist, elevating lifelong susceptibility to chronic diseases [6]. Recent research has expanded beyond individual nutrients to examine broader dietary patterns and indices, such as the Dietary Inflammatory Index (DII), for their association with chronic inflammation [7, 8]. The DII quantifies the inflammatory potential of a diet based on multiple food components, offering a tool for healthcare professionals to guide individuals toward anti-inflammatory eating habits. While the DII has proven helpful in guiding dietary interventions for adults, its application in pediatric populations remains underexplored, particularly concerning metabolic outcomes [9, 10].

Concurrently, spexin has garnered attention as a novel adipokine with pleiotropic roles in regulating body weight, appetite, and metabolic homeostasis [11]. This pleiotropic peptide appears to regulate multiple metabolic processes, including body weight control, satiety signaling, and glucose/lipid homeostasis [12–14]. Some other studies evaluated spexin's association with some inflammatory biomarkers [12, 15, 16]. Therefore, spexin has been proposed as a favorable biomarker for cardiometabolic diseases. Kumar et al. showed that obese adolescents with higher serum C-reactive protein (CRP) were more susceptible to higher leptin levels and lower spexin levels, suggesting that spexin levels might be related to the risk of cardiovascular disease (CVD) [17]. The relationship between inflammation and metabolic dysfunction appears early in life, as evidenced by CRP's association with preclinical atherosclerotic changes [18]. It seems that spexin status has a potential role in the early development of CVD and diabetes [19]. Several human studies have shown the inverse relationship between spexin and leptin and the direct relationship between spexin and ghrelin, obestatin, and adiponectin [20].

For the first time, this study investigates the relationships between DII, circulating spexin levels, appetite regulation, and inflammatory biomarkers in children and adolescents. Addressing critical gaps in pediatric research, we also examine how DII associates with metabolic syndrome components, insulin resistance, and obesity parameters, providing comprehensive insights into early metabolic dysfunction.

Materials and methods

Study participants

This analytical observational study included 190 children and adolescents (10–18 years), comprising 95 obese and 95 normal-weight individuals, who were recruited from urban health centers and through public advertisements. Among them, 180 participants (90 obese and 90 normal-weight) provided complete dietary and anthropometric data. A further subset of 90 adolescents (45 obese and 45 normal-weight) agreed to and provided fasting blood samples for the measurement of spexin, inflammatory markers, and other biochemical parameters **(**Fig. 1**)**. Participation required voluntary assent and parental consent. Exclusion criteria consisted of a medical history of cancer, inflammatory diseases (including cardiovascular, neurological, respiratory, or gastrointestinal disorders), metabolic or endocrine abnormalities, adherence to restrictive diets (e.g., vegetarian

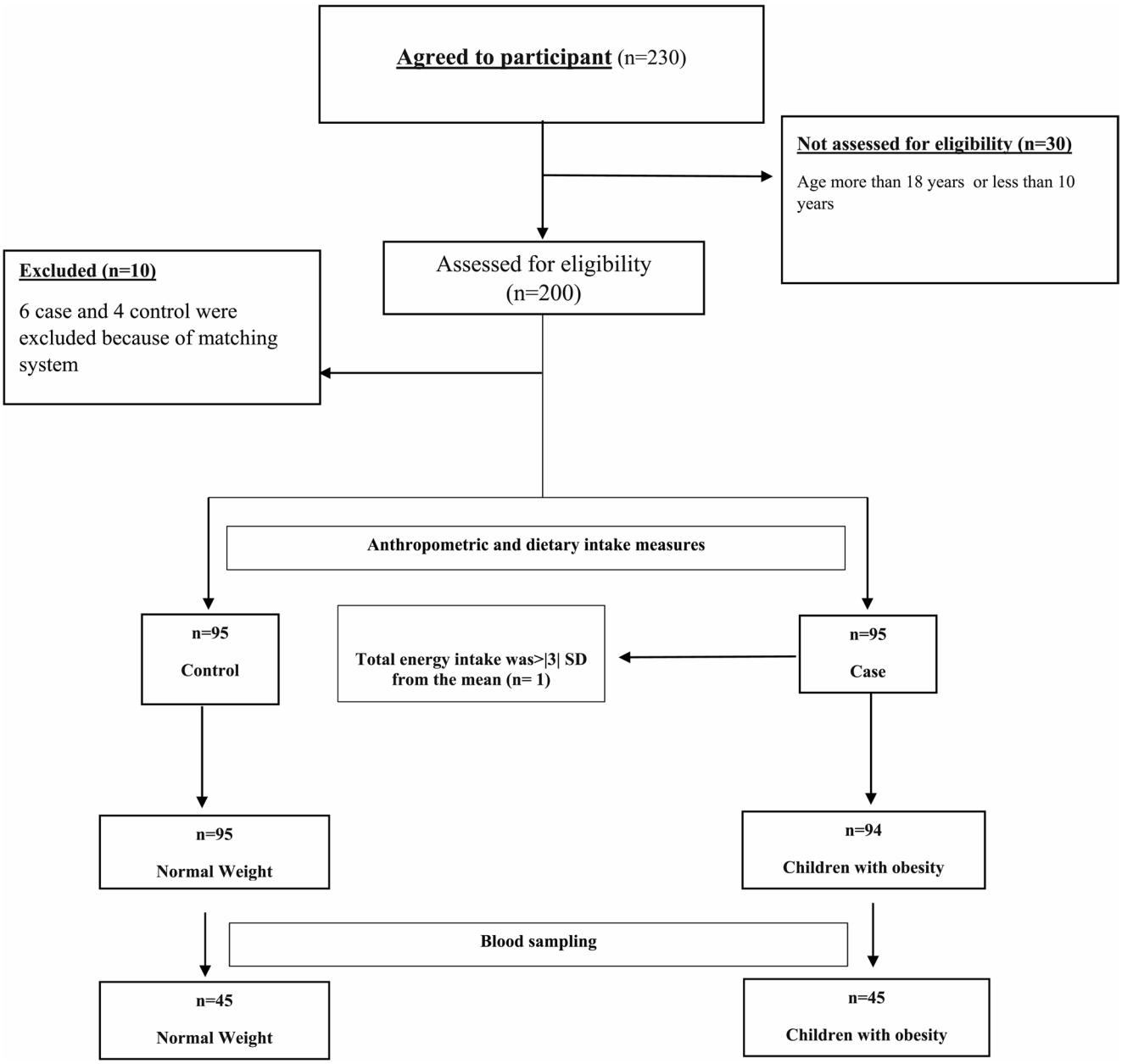

Fig. 1 Flowchart of study

or calorie-restricted diets), or suspected genetic obesity syndromes (e.g., Prader-Willi syndrome). Body weight status was defined using the Centers for Disease Control and Prevention (CDC) growth charts (2000). Normal weight was defined as a BMI between the 5th and 85th percentiles for age and sex, whereas obesity was defined as a BMI≥95th percentile. The CDC charts were selected for this study due to their established use in prior national health surveys in Iran, allowing for comparability with local data. All participants and their legal guardians were fully informed of the study's aims and protocols and provided written informed consent before inclusion.

Sample size calculation

For sample size estimation, we utilized data from Asghari et al. [21] with PS software, calculating a required sample of 180 participants (odds ratio (OR): 0.35 [0.14–0.39]; baseline probability [P_0]: 0.3; power: 80%). However, as not all 180 eligible children and adolescents consented to blood sampling, a separate sample size calculation was performed for biochemical analyses. This secondary calculation, based on spexin levels (mean ± SD) from Kumar et al. [22], determined that 81 participants would be required ($\Delta = 0.13$; $\sigma = 0.21$; $m = 1$; power = 80%). Accounting for an 11% attrition

rate, the final target sample size for biochemical testing was set at 90 participants.

Data collection

Height was measured to the nearest 0.5 cm using a wall-mounted stadiometer with participants standing barefoot. Body weight was assessed using a calibrated SECA 707 digital scale (range: 0.1–150 kg, precision ± 0.1 kg) while participants wore light clothing. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Body composition analysis was performed using bioelectrical impedance analysis (Tanita MC-780 MA, Amsterdam, Netherlands). Blood pressure measurements were obtained using a mercury sphygmomanometer after 15 min of rest in a supine position, with appropriate cuff sizes selected for each participant. Both systolic (SBP) and diastolic blood pressure (DBP) were recorded. Appetite parameters were evaluated using a 100-mm visual analog scale (VAS) with bipolar anchors representing extreme positive and negative ratings. The scale measured: [1] hunger [2], satiety [3], fullness [4], prospective food consumption, and [5] desire for specific food types (fatty, salty, and sweet foods) [23]. Psychological distress was evaluated using the Depression Anxiety Stress Scales-21 (DASS-21), a validated short-form instrument demonstrating good reliability and validity in Iranian adolescent populations. This 21-item scale provides separate measures of depression, anxiety, and stress symptoms through three 7-item subscales [22]. Physical activity levels were assessed using the Modifiable Activity Questionnaire (MAQ). The Persian version of this instrument demonstrated acceptable psychometric properties in adolescent populations, with test-retest reliability of 97% (intraclass correlation coefficient) and criterion validity of 49% (compared to accelerometer data) [24]. Pubertal development was evaluated using the Tanner staging method. Following a standardized explanation of the five developmental stages, participants were presented with gender-appropriate pictorial representations and instructed to select the image that most closely matched their current physical development [25].

All 180 participants (90 obese and 90 normal-weight) provided complete food frequency questionnaire (FFQ) responses, anthropometric, and body composition data. From this group, a subset of 90 adolescents (45 obese and 45 normal-weight) consented to blood sampling. Following a 12-hour overnight fast, blood was collected from this subset for biochemical analysis. Serum concentrations of interleukin-10 (IL-10), interleukin-1-beta (IL-1β), and spexin were quantified using commercially available ELISA kits (Bioassay Technology Laboratory; Shanghai Korean Biotech Co., Ltd) according to the manufacturer's protocols. High-sensitivity C-reactive protein (hs-CRP) levels were determined via turbidimetric assay. Lipid profiles were assessed using enzymatic colorimetric methods (Pars-Azmoon Co., Tehran, Iran) for HDL-cholesterol (HDL-C), triglycerides (TG), and fasting blood glucose (FBG). Serum insulin levels were measured by ELISA (Monobind, Lake Forest, CA, USA). Insulin resistance was estimated using the homeostasis model assessment (HOMA-IR) index, calculated as [26]:

HOMA-IR = [fasting insulin (μIU/ml) × fasting glucose (mg/dl)]/405.

Metabolic syndrome diagnosis

Metabolic syndrome (MetS) was diagnosed according to modified Cook criteria [27], requiring the presence of ≥ 3 of the following components:

1. Low HDL-cholesterol (< 40 mg/dL).
2. Elevated triglycerides (≥ 110 mg/dL).
3. Impaired fasting glucose (≥ 110 mg/dL; ADA criteria [28])
4. Abdominal obesity (waist circumference ≥ 90th percentile for age/sex [29])
5. Elevated blood pressure (≥ 90th percentile for sex, age, and height [30])

Dietary assessment

Trained nutritionists administered a validated 168-item semi-quantitative FFQ to assess participants' habitual dietary intake over the preceding 12-month period. This instrument has demonstrated acceptable reliability and validity for dietary assessment in adolescent populations, as established in previous validation studies [31]. Participants reported consumption frequencies (daily, weekly, monthly, or annually) for each food item using standardized Iranian portion sizes. Parental assistance was utilized to enhance the recall accuracy of food types and quantities. Reported intakes were converted to daily gram amounts using Iranian household measures.

Nutrient analysis was performed using modified Nutritionist IV software (v3.5.2), with energy and nutrient values derived from the FFQ data. These data were subsequently used to calculate DII scores, with calculation methods following established protocols [9]. The DII was computed using a standardized algorithm developed through a systematic review of studies (1950–2010) linking dietary components to six inflammatory biomarkers (IL-1β, IL-4, IL-6, IL-10, CRP, TNF-α). Each of the 26 food parameters,

including energy, carbohydrates, protein, total fat, fiber, and saturated, monounsaturated, polyunsaturated, omega 3 and omega 6 polyunsaturated fatty acids, cholesterol, iron, magnesium, zinc, selenium, vitamins A, B1, B2, B3, B6, B12, C, D, E, folic acid, β-carotene, and caffeine was assigned an inflammatory effect score based on published evidence: anti-inflammatory (− 1), neutral (0), or pro-inflammatory (+ 1). These scores were weighted by study quality and converted to proportions (0–1 scale) centered around zero. Normalized values were multiplied by their respective inflammatory effect scores to generate food parameter-specific scores, which were summed to derive individual DII scores. Higher positive values indicated greater pro-inflammatory potential, while lower negative values reflected anti-inflammatory potential. Energy-adjusted DII (E-DII) scores were computed using the residual method. Participants were stratified into DII tertiles: T1 (anti-inflammatory, <−1.62), T2 (intermediate, − 1.62 to 0.80), and T3 (pro-inflammatory, ≥ 0.80).

Statistical analysis

Statistical analyses were conducted using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated using Skewness-Kurtosis tests. Normally distributed quantitative variables were expressed as mean±standard deviation, while non-normally distributed variables were reported as median (interquartile range). Group comparisons were performed using independent samples t-tests for parametric data and Mann-Whitney U tests for non-parametric data. Categorical variables presented as frequencies (percentages) were analyzed using chi-square tests. Logistic regression models were employed to calculate odds ratios (ORs) with 95% confidence intervals (CIs) across three sequential models: an unadjusted crude model (Model 1), a model adjusted for demographic factors including sex, age, pubertal stage, and stress levels (Model 2), and a fully adjusted model incorporating total caloric intake (Model 3). Associations between DII tertiles (using the highest tertile as reference) and biomarkers (including spexin and inflammatory markers) and appetite measures were examined using general linear models, adjusted for potential confounders including BMI, age, sex, pubertal stage, and physical activity level. Pearson correlation coefficients were computed to assess bivariate relationships between DII scores and specific inflammatory biomarkers (IL-1β, IL-10, and hs-CRP).

Results

The characteristics of the 189 participants (95 normal-weight and 94 with obesity) included in the final analysis are presented in Table 1. The flow of participants, detailing the recruitment and the subsets for dietary and biochemical studies, is illustrated in Fig. 1. DII scores ranged from −4 (most anti-inflammatory) to +3 (most pro-inflammatory), with an overall mean (SD) of −1.25 (1.01). Notably, all metabolic subgroups (those with MetS, elevated triglycerides, low HDL-cholesterol, high hs-CRP, abdominal obesity, insulin resistance, or hyperinsulinemia) demonstrated

Table 1 Demographic, Anthropometric Characteristics, and Dietary Intakes of the Study Participants

	Normal Weight	Obesity	P-value[†]
	Mean (SD)	Mean (SD)	
Number	95	94	
Age	13.78 (3.02)	13.92 (2.98)	0.830
Birth Weight(gr)	3164.10 (701.51)	3297.39 (612.50)	0.222
Physical Activity (MET-h/week)	14.01 (5.31)	15.21 (7.25)	0.372
Calorie intake (Kcal/day)	2079.89 (654.83)	2340.26 (675.35)	0.006
Protein intake (g/day)	67.79 (24.62)	77.20 (22.22)	0.005
Carbohydrate intake (g/day)	302.97 (95.61)	337.67 (110.9)	0.011
Total fat intake (g/day)	71.11 (27.76)	77.57 (26.14)	0.081
[&*]Appetite VAS score	36 (11.25)	36 (11.00)	0.503
BMI (kg/m^2)	18.92 (3.57)	28.34 (4.14)	<0.001
WC (cm)	71.7 (11.71)	93.10 (11.96)	<0.001
SBP (mmHg)	101.70 (10.55)	109.90 (11.82)	0.023
DBP (mmHg)	65.75 (12.50)	64.75 (14.10)	0.831
Fat mass (%)	20.17 (6.98)	32.80 (6.26)	<0.001
FFM (kg)	36.14 (10.93)	46.08 (13.63)	<0.001
[% $]Depression status			
Normal	80 (84.4)	80 (85.1)	0.951
Low	7 (7.3)	8 (8.5)	
Medium	7 (7.3)	5 (5.3)	
Sever	1 (1)	1 (1.1)	
[% $]Anxiety status			
Normal	68 (70.8)	75(79.8)	0.327
Low	17 (18.8)	10 (10.7)	
Medium	6 (6.3)	7 (7.4)	
Sever	4 (4.2)	2 (2.1)	
[% $]Stress Status			
Normal	83 (87.3)	82 (87.2)	
Low	11 (11.5)	9 (9.6)	
Medium	1 (1.2)	3 (3.2)	0.544
[% $]Pubertal stage			
Pre- pubertal	21 (22.1)	12 (12.7)	0.194
Pubertal	53 (55.8)	55 (58.5)	
Post-pubertal	21 (22.1)	27 (28.8)	

Abbreviations: BMI: Body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: Diastolic blood pressure; FFM: Fat-free mass

[†]Independent Sample Test or [&] Mann-Whitney U Test for Quantitative variables, [%]chi2 Test for Categorical variables*Median (IQR), [$]N (%)

negative mean DII scores. As shown in Table 1, participants with obesity had significantly higher adiposity measures (fat mass percentile, waist/hip circumference; all $p<0.001$) and greater caloric, protein, and carbohydrate intake (all $p<0.05$) compared to normal-weight controls, despite similar mean ages (13.66±2.77 years) across groups.

Table 2 revealed a significantly elevated risk of obesity with higher DII scores (>−1.35 vs. ≤−1.35) across all models: crude (OR: 1.79, 95%CI 1.03–3.15, $p=0.04$), model 2 adjusted for demographic factors (OR: 2.11, 95%CI 1.17–3.83, $p=0.01$), and model 3 fully-adjusted for sex, age, maturity, stress level, total dietary calorie intake, and physical activity (OR: 2.03, 95%CI 1.10–3.75, $p=0.02$). No significant associations were observed between DII and MetS, its individual components (elevated triglycerides, low HDL-cholesterol, elevated systolic blood pressure, or high waist circumference), or insulin resistance in any of the models.

Table 3 demonstrates the relationships between DII tertiles and biomarkers. In the crude model, participants in the most anti-inflammatory DII tertile (T1: ≤−1.62) had significantly higher spexin levels (β=79.49, 95%CI 0.11–158.93.11.93, $P=0.048$), higher IL-10 levels (β=260.27, 95%CI 4.33–516.20, $P=0.04$), and lower appetite scores (β=−3.03, 95%CI −5.80 to −0.24, $P=0.03$) compared to the pro-inflammatory reference tertile (T3: >−0.8). However, after adjustment for BMI, age, sex, pubertal stage, and physical activity, these associations for IL-10 (β=214.42, 95%CI −42.27 to 471.16, $P=0.08$), appetite score (β=−2.58, 95%CI −5.47 to 0.30, $P=0.07$), and spexin (β=74.42, 95%CI −7.33 to 155.38, $P=0.052$) were no longer statistically significant, though the association with spexin suggested a large effect size approaching significance. No significant associations were found between DII tertiles and hs-CRP or IL-1β in either crude or adjusted models.

As shown in Table 4, Pearson correlation analysis revealed a significant positive correlation between the continuous DII score and hs-CRP levels (r=0.30, P=0.005). No significant correlations were observed between DII and IL-1β or IL-10.

Table 2 The association of DII with obesity, insulin resistance, and metabolic syndrome and its components in children

	Dietary Inflammatory Index OR (95% CI)		P-value[†]
	DII≤ −1.35	DII> −1.35	
Obesity			
Model 2 [**]	1.00 (ref)	2.11 (1.17–3.83.17.83)	0.01
Model 3[***]	1.00 (ref)	2.03(1.10–3.75.10.75)	0.02
MetS			
Model 1 [*]	1.00 (ref)	2.48 (0.63–9.75.63.75)	0.19
Model 2 [**]	1.00 (ref)	3.55 (0.80–15.74.80.74)	0.09
Model 3[***]	1.00 (ref)	4.96 (0.91–26.98.91.98)	0.06
TG≥ 110 mg/dL			
Model 1 [*]	1.00 (ref)	1.84 (0.76–4.45.76.45)	0.17
Model 2 [**]	1.00 (ref)	2.09 (0.79–5.49.79.49)	0.13
Model 3[***]	1.00 (ref)	2.49 (0.89–6.93.89.93)	0.08
HDL-C< 40 mg/dL.			
Model 1 [*]	1.00 (ref)	2.09 (0.72–6.01.72.01)	0.17
Model 2 [**]	1.00 (ref)	3.24 (0.99–1.83.99.83)	0.05
Model 3[***]	1.00 (ref)	3.07 (0.86–10.87.86.87)	0.08
SBP≥ 90th percentile			
Model 1 [*]	1.00 (ref)	2.58 (0.50–13.24.50.24)	0.25
Model 2 [**]	1.00 (ref)	6.66 (0.73–60.69.73.69)	0.09
Model 3[***]	1.00 (ref)	6.98 (070-69.38.38)	0.09
WC≥ 90th percentile			
Model 1 [*]	1.00 (ref)	1.40 (0.66–2.96.66.96)	0.37
Model 2 [**]	1.00 (ref)	1.41 (0.65–3.06.65.06)	0.37
Model 3[***]	1.00 (ref)	1.30 (0.59–2.86.59.86)	0.51
[#]Insulin Resistance			
Model 1 [*]	1.00 (ref)	2.54 (0.64–9.92.64.92)	0.18
Model 2 [**]	1.00 (ref)	2.88 (0.69–11.91.69.91)	0.14
Model 3[***]	1.00 (ref)	2.37 (0.54–10.32.54.32)	0.24

Abbreviations: MetS: metabolic syndrome; WC: waist circumference; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; SBP: systolic blood pressure[†]Binary logistic regression[*] Crude[**] Adjusted for sex, age, maturity, and stress level,[***] model2 + total dietary calorie intake + Physical Activity Level[#]HOMA-IR cut-off values for insulin resistance were calculated to be 2.67 (sensitivity 88.2%, specificity 65.5%) in boys and 2.22 (sensitivity 100%, specificity 42.3%) in girls in the prepubertal period, and 5.22 (sensitivity 56%, specificity 93.3%) in boys and 3.82 (sensitivity 77.1%, specificity 71.4%) in girls in the pubertal period

Discussion

The current study investigated the relationship between DII score and spexin, obesity, appetite, MetS and its components, insulin resistance, and some inflammatory biomarkers, in the Iranian children/adolescent population. To our knowledge, this study was the first attempt to assess the relationship between DII, spexin levels, and appetite scores in children with obesity. In our study, the mean (SD) of children's DII score was − 1.25 (1.01). Notably, the mean (SD) of the DII score was negative in both sub-groups of children. Furthermore, the odds of obesity increased with the increase in DII. The relationship between obesity and inflammation has been hypothesized to be reciprocal. However, little evidence has been published on obesity due to previous inflammatory status [32]. Several studies have recently investigated the correlation between DII and obesity in adults. Despite the contradictions, some of these

Table 3 Relationships between DII textiles and spexin, appetite, and some inflammatory biomarkers

	Crude model			**Adjusted model	
		B (95%CI)	*P-value	B (95%CI)	*P-value
Spexin	Tertile1	79.49 (0.11 - 158.93)	0.048	74.42 (−7.33 - 155.38)	0.051
	Tertile2	−12.33 (−82.26 - 57.59)	0.72	−7.46 (−0.79 - 64.93)	0.841
	Tertile3	Ref		Ref	
Appetite score	Tertile1	−3.03 (−5.80 - −0.24)	0.03	−2.58 (−5.47 - 0.30)	0.071
	Tertile2	−2.01 (−4.79 - 0.76)	0.15	−1.98 (−4.83 - 0.87)	0.170
	Tertile3	Ref		Ref	
IL-10	Tertile1	260.27 (4.33 - 516.20)	0.04	214.42 (−42.27 - 471.16)	0.084
	Tertile2	53.65 (−171.36 - 278.62)	0.63	47.22 (−178.80 - 273.24)	0.641
	Tertile3	Ref		Ref	
hs-CRP	Tertile1	−0.53 (−1.98 - 0.91)	0.83	−0.2 (−1.56 - 1.62)	0.770
	Tertile2	−0.25 (−1.52 - 1.02)	0.70	−0.32 (−1.52 - 0.87)	0.591
	Tertile3	Ref			
IL-1β	Tertile1	445.06 (−319.71 - 1209.8)	0.25	325.177 (−445.32 - 1098.68)	0.401
	Tertile2	146.48 (−525.9 - 818.87)	0.66	102.63 (−575.72 - 781.10)	0.702
	Tertile3	Ref			

Abbreviations: DII: Dietary Inflammatory Index; hs-CRP: high-sensitivity C-reactive protein; IL: interleukin*GLM (general linear model)**Adjusted for BMI, age, sex, and pubertal stage Physical Activity LevelTertile1: DII≤ −1.62; Tertile2: −1.62<DII≤ −0.8; Tertile3: DII> −0.8

Table 4 Associations of DII score with inflammatory biomarkers

Parameters	r	#P-value
IL-1beta	0.139	0.201
Il-10	−0.12	0.230
Hs-CRP	0.30	0.005

Abbreviations: DII: Dietary Inflammatory Index; hs-CRP: high-sensitivity C-reactive protein; IL: interleukin.

#Data presented as Pearson correlation coefficient (r)

studies admitted the role of a high DII score in the obesity outbreak [33]. Our findings in children were aligned with a meta-analysis that examined the association between DII and obesity in human adults, suggesting that adherence to a high DII score could increase BMI and obesity [34].

Moreover, several animal models have shown the effect of inflammatory cytokines on the propensity to gain extra weight [35]. The mechanisms by which a pro-inflammatory diet induces obesity remain unclear. In this regard, possible mechanisms include the stimulation of appetite by pro-inflammatory cytokines, such as interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor alpha (TNF-α) [36]. Specific nutrients can also activate hypothalamic inflammation, which can consequently cause obesity [37]. Also, the diet's effect on changes in the intestinal microbiota is another possible explanation that precedes low-grade inflammation, which elevates adiposity [38].

Moreover, in our study, there was no significant association between DII and MetS and its components. The promising finding of the present study was that subjects with the lowest DII score (indicating an anti-inflammatory diet) had higher spexin and IL-10 levels and lower appetite scores compared to those with the highest DII score (indicating a pro-inflammatory diet). Spexin is a novel endogenous adipokine widely expressed in the central nervous system and peripheral tissues [11]. Moreover, it plays a pivotal role in obesity pathogenesis, immune system function, energy, and glucose and lipid metabolism. Some literature confirmed the protective effect of diets (including diet-induced obesity) on spexin levels. It has been proposed that an imbalance in spexin secretion can play a role in obesity complications. According to previous studies, circulating spexin and its expression in adipose tissue are remarkably decreased in subjects with obesity [12, 39, 40]. In our previous study, circulating spexin was significantly lower in children with obesity and high-fat mass compared to the control group [14]. Significant correlations between spexin and some inflammatory biomarkers have been reported in some studies [13, 17]. Kumar et al. found that participants with higher hs-CRP (≥ 3 mg/L) had 12.25 times more chance of having 'low spexin and high leptin' than participants with lower hs-CRP [17]. In one recent study, a higher spexin level leads to a reduction in the expression of IL-1β, IL-6, and TNFα and an improvement in IL-10. Spexin improved macrophage recruitment and adipose tissue inflammation in obese mice [41]. In our previous study, obese children had significantly higher hs-CRP and lower IL-10 than normal-weight children. Also, serum spexin was significantly correlated with IL-10 [14]. Among subjects with higher hs-CRP, higher DII scores reflect a more pro-inflammatory diet. Considering the observed relationship between DII, spexin, IL10, and appetite score, and combining these findings with our previous study results, there is a suggestion of a possible association among DII, spexin, and IL10, warranting further investigation.

In addition to the spexin levels, children with lower DII values had a significantly lower appetite score, indicating that following a more anti-inflammatory diet (rich in fruits and vegetables) leads to this reduction. According to previous studies, pro-inflammatory cytokines, including IL-1, IL-6, and TNF-α, can cause appetite stimulation [36]. Indeed, people who have better control over their eating habits and physical activity to lose weight tend to consume healthier foods like fruits and vegetables. There are many studies regarding the relationship between other nutritional indices and appetite. For example, greater adherence to the DASH diet has been proven to reduce appetite and promote weight loss. These effects have been attributed to factors such as the consumption of nuts, low-fat dairy products, and fish, which play a role in increasing satiety and reducing appetite [42]. Another valuable finding of the current study was a positive association of DII score with hs-CRP levels. Several studies on adults reported that a high score on the DII is associated with inflammation biomarkers such as CRP, IL-6, homocysteine, and TNF-α [43]. Khan et al. reported a higher CRP value for children in level three of the DII compared to those in level one [44]. In another study on the pediatric group, higher DII was associated with a significant increase in various inflammatory markers, including TNF-α, IL-1, and IL-2 [45]. Therefore, this finding suggests that a pro-inflammatory diet can be considered an independent risk factor for obesity incidence. In this regard, it is crucial to find preventive approaches and educate people as a noble solution to diminish the complications resulting from obesity. Some study limitations should be mentioned: 1- The limitations of the FFQ in the dietary assessment also apply to the DII score. However, we employed a trained health professional to interview the participants instead of the self-employed FFQ to increase the validity of the data. 2- The DII was calculated using data on only 26 nutrients and food components. Despite the limitation in the number of parameters, the DII score was successfully associated with some of the inflammatory markers. The Children's Dietary Inflammatory Index, designed and validated for the age range of 6 to 14 years, includes 25 food items. These items are very similar to our parameters, except for caffeine. Given the older age of our participants, it seems reasonable to consider caffeine sources. 3- The use of CDC growth charts, while common in regional studies, may not be as universally representative as the World Health Organization (WHO) growth standards. Future studies could benefit from using WHO references to facilitate broader international comparisons.

Conclusions

In conclusion, this study demonstrates that a pro-inflammatory diet, as indicated by higher DII scores, is significantly associated with an increased risk of obesity and higher levels of the inflammatory marker hs-CRP in children. While the initial associations between an anti-inflammatory diet and higher spexin, higher IL-10, and lower appetite were observed, these relationships were no longer significant after accounting for key confounders. This suggests that the link between diet and these biomarkers may be complex and interrelated with overall adiposity. The primary effect of a pro-inflammatory diet appears to be a direct association with general obesity and systemic inflammation (hs-CRP), rather than a direct effect on the specific components of MetS in this cohort. These results underscore the importance of promoting anti-inflammatory dietary patterns from an early age to help mitigate obesity risk and its inflammatory complications.

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Author contributions This study was conceptualized by AO and MB. Data collection was performed by MB, SH, and JM. Formal analysis was conducted by MB and JM, and funding acquisition was by MB. The investigation was carried out by MB, SH, and AO The methodology was set by MB and SH. The study was supervised by AO and MB. Writing of the original draft was performed by MB, SH, and JM. Reviewing and editing were carried out by AO, MB, SH, FB, and JM.

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Data availability All data is available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate Ethics approval was obtained from the research ethics committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1397.179). All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all subjects or parents on behalf of the children after explaining the objective of the study to participants.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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