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Obesity and IL-21, IL-22, and IL-23 in low-grade inflammation: associations with nutrition and stimulant use

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Abstract

Introduction: *Interleukin (IL)-21, IL-22, and IL-23 have been most frequently evaluated in patients with autoimmune or inflammatory diseases. In contrast, data on these cytokines in obesity and obesity-related low-grade inflammation remain limited.*

Material and methods: *Serum concentrations of IL-21, IL-22, and IL-23 were analyzed in 84 obese individuals. Dietary intake was assessed using a nutrition questionnaire and a 3-day food diary. Body composition was evaluated using bioelectrical impedance analysis.*

Results: *Within the obese cohort, IL-23 levels were negatively associated with body mass index (BMI). Alcohol consumption was associated with lower circulating IL-21 levels, while self-reported physical activity was associated with higher IL-23 concentrations. Dietary factors, including the amount and type of carbohydrates, dietary glycemic index, and the frequency of consumption of selected food groups (wholemeal pasta, fast food, cottage cheese, eggs, and fish), showed associations with circulating IL-21, IL-22, and IL-23 levels. In addition, dietary intake of retinol, niacin, riboflavin, omega-3 fatty acids, and β-carotene was associated with variability in the concentrations of the studied cytokines.*

Conclusions: *In obese individuals without autoimmune diseases, circulating IL-23 levels showed a negative association with BMI. Circulating levels of IL-21, IL-22, and IL-23 were associated with selected lifestyle and dietary factors, including alcohol consumption, physical activity, dietary patterns, and nutrient intake. These findings should be interpreted as exploratory and hypothesis-generating.*

Key words: *obesity, diet, nutrients, adipocytes, IL-21, IL-23, IL-22, low-grade inflammation.*

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Introduction

Obesity is associated with chronic inflammation. Adipose tissue is an endocrine/paracrine organ and secretes pro-inflammatory cytokines that have been associated with adverse systemic effects [1]. Studies in a mouse model have shown that obesity induced low-grade inflammation is associated with Th17 cell differentiation, promoted by interleukin (IL)-23 [1]. Th17 cells play an essential role in various inflammatory diseases, including autoimmunity [2]. An increased number of Th17 lymphocytes has been associated with enhanced production of Th17-derived cytokines, including IL-17, IL-21, and IL-22. T helper 17 cells are thought to orchestrate inflammatory responses through complex interactions involving IL-17, IL-21, IL-22, and IL-23 [3]. Research has more often focused on the role of IL-21, IL-22, and IL-23 in the pathogenesis of diseases such as psoriasis, rheumatoid arthritis (RA), diabetes, asthma, neurodegenerative diseases, irritable bowel syndrome, or cancer. Many studies have shown that obesity is a risk factor for the above-mentioned diseases, which may indicate a similarity in changes in the cytokine network associated with the pathogenesis of obesity and these diseases [4-6]. There is still a lack of data on the levels of IL-21, IL-22, and IL-23 among obese subjects without autoimmune disease and their role in the development of low-grade inflammation.

Interleukin 21 is produced by activated T helper cells (Th1, Th2, Th17), follicular T helper cells (Tfh), and NKT cells. It plays a key role in enteritis, psoriasis, type I diabetes, systemic lupus erythematosus (SLE), and RA [7]. This cytokine is characterized by a dual role and pro-inflammatory and anti-inflammatory effects. IL-21 regulates the innate and adaptive (both humoral and cellular) immune response, thus affecting a wide range of lymphoid, myeloid, and epithelial cells [8]. Higher expression of IL-21 and IL-21R mRNA has been demonstrated in adipose tissue from obese animals consuming a high-fat diet (HFD) and in the stromal vascular fraction collected from

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obese humans, in parallel with macrophages and inflammatory markers [9].

Interleukin 22 belongs to the IL-10 cytokine superfamily. It is involved in antibacterial, inflammatory, and tissue repair processes, depending on the environment of cytokine expression. IL-22 is produced by innate and adaptive immune cells and is involved in inflammation, infection, autoimmunity, and tissue homeostasis [10]. Studies confirm the bidirectional effect of IL-22, indicating the anti-inflammatory and pro-inflammatory role. This cytokine plays a protective role in controlling lung epithelial damage or intestinal inflammation [11, 12]. It should be mentioned that the influence of the microbiota on increasing the level of IL-22 has a beneficial effect on metabolic inflammation and, at the same time, a diet rich in fiber has a beneficial effect in this regard [13].

Interleukin 23 is produced by dendritic cells (DC) and activated macrophages and therefore by activated antigen-presenting cells. IL-23 plays an important role in the development, differentiation, and maintenance of Th17 cells, but also influences the pathogenicity of Th17 cells by interacting with IL-17 and tumor necrosis factor α (TNF-α), increasing inflammation. IL-23 can also play a dual role, both pro-inflammatory and anti-inflammatory [10]. IL-23 plays a key role in the pathogenesis of meta-inflammatory diseases. Adipose IL-23 transcripts were found to increase in individuals with high concentration of low-density lipoprotein cholesterol (LDL-c) compared to the low LDL-c group [14].

The aim of the study was to analyze the relationship between the level of obesity, the amount of adipose tissue or its distribution, and the concentrations of IL-21, IL-22, and IL-23 in the blood of obese people. At the same time, it was important to assess the impact of dietary habits, food groups, nutrients, and physical activity, on the levels of IL-21, IL-22, and IL-23 in obese subjects. The relationships related to dietary factors, obesity, and low-grade inflammation and these three interleukins are still not explained.

Table 1. Age characteristics of the study population

Variable	Value
n	84
Age (years), min.-max.	18-73
Age (years), Me [min.-max.]	39.5 [33.8-51.0]
Age (years), mean ±SD	41.4 ±12.1
Participants < 30 years, *n* (%)	12 (14.3)
Participants 30-44 years, *n* (%)	37 (44.0)
Participants 45-60 years, *n* (%)	29 (34.5)
Participants > 60 years, *n* (%)	6 (7.1)

n – number of observations, mean – arithmetic mean, SD – standard deviation, Me – median, min. – minimum, max. – maximum

Material and methods

Ethics

The project was approved by the Institutional Bioethics Committee (Resolution No. 10/04/2017). All participants voluntarily agreed to participate in the study by signing the required documents including informed consent.

Subjects

The research was carried out in a group of 84 people (62 women and 22 men) with a body mass index (BMI) equal to or greater than 30 kg/m^2. The study included 84 participants aged 18 to 73 years. The median age of the cohort was 39.5 years (interquartile range [IQR]: 33.8-51.0), indicating a predominance of middle-aged adults. Participants aged 30-44 years constituted the largest age group (44.0%), followed by those aged 45-60 years (34.5%). Younger (< 30 years) and older (> 60 years) individuals represented smaller subgroups (14.3% and 7.1%, respectively) (Table 1). The BMI of the examined population ranged from 30.0 to 58.1 kg/m^2, with an average of 36.65 ±5.27 kg/m^2. There were 34 (40.5%) persons with obesity classes I and II, respectively and 16 (19.0%) with class III obesity. At the time of examination, 21 subjects (25.0%) reported having arterial hypertension, 3 (3.6%) had non-alcoholic fatty liver disease (NAFLD), 6 (7.1%) were being treated for hypothyroidism, and 2 for atherosclerosis. Among the respondents, 21 were treated with blood pressure lowering drugs, 10 with β-blockers, 4 with levothyroxine, and 3 used nonsteroidal anti-inflammatory drugs (NSAIDs) on an as-needed basis. The respondents included a group of 29 (34.5%) who occasionally took dietary supplements and 11 (13.1%) who regularly supplemented vitamin D_3. Lack of preparation for the study and an incorrectly completed questionnaire or nutritional diary resulted in exclusion from the study.

Blood sampling and laboratory analysis

Fasting blood samples were collected between 7:00 and 9:00 am. After centrifugation for 10 minutes at 4^{o}C, the serum was aliquoted into tubes and frozen at –86^{o}C. The concentrations of IL-21, IL-22, and IL-23 were analyzed using a commercially available kit using the multiplex test method based on Milliplex MAP Kit magnetic beads (Merck Millipore, USA) and the FLEXMAP3D system (Merck Millipore, USA).

Height and body composition measurements

Height was measured twice with an accuracy of 0.5 cm using a Tanita HR-001 stadiometer (TANITA, Tokyo, Japan). The average of these measurements was used in the second part of the study. Body composition was analyzed using the non-invasive method of bioelectrical impedance analysis (BIA) with variable frequencies. The tool

used for this purpose was the variable frequency analyzer (5 kHz, 50 kHz and 250 kHz MC) 780 MA (TANITA, Tokyo, Japan), equipped with four pairs of electrodes.

Lifestyle and nutrition assessment

Respondents completed the author's questionnaire on comorbidities, medications taken, supplements and lifestyle, including physical activity, number of meals, addictions and frequency of coffee and tea consumption. This survey was enriched with a food frequency questionnaire, which highlights products with anti-inflammatory properties [15]. Before reporting to the study, each participant had to complete a food diary containing 3 days (2 working days, 1 weekend) of usual nutrition. The acquired food diary was calculated using the nutrition calculator.

Statistical analysis

Statistical analyses were performed using Statistica version 13.1 (StatSoft, Poland). The distribution of continuous variables was assessed using the Shapiro-Wilk test. As cytokine concentrations exhibited non-normal and left-censored distributions, exclusively nonparametric statistical methods were applied. Continuous variables are reported primarily as median with IQR, and, where appropriate, minimum and maximum values. Mean ± standard deviation is provided only for descriptive characteristics of the study population and not for cytokine concentrations. Differences between two independent groups were assessed using the Mann-Whitney *U* test. Associations between continuous variables were evaluated using Spearman's rank correlation coefficient (ρ), with the exact paired sample size (*n*) reported for each analysis. For categorical variables, Pearson's chi-square test was applied. Effect sizes are presented as Spearman's ρ for correlation analyses, together with corresponding *p*-values. The level of statistical significance was set at $p < 0.05$. Given the exploratory nature of the study and the large number of statistical tests performed, the findings should be interpreted with caution due to the increased risk of type I error.

Results

Cytokine concentrations in the study population

To examine associations between lifestyle factors and interleukins involved in obesity-related low-grade inflammation, circulating levels of IL-21, IL-22, and IL-23 were analyzed in relation to body composition parameters and data obtained from the FFQ-6 questionnaire, three-day food diaries, and the author-designed survey. Table 2 summarizes the circulating concentrations of IL-21, IL-22, and IL-23 in the study population, including median values, interquartile ranges, and minimum and maximum concentrations. Detectable levels of the analyzed interleukins were not observed in all participants.

Table 2. Circulating cytokine levels in the study population

Interleukin	*n*	Median [IQR]	Min.	Max.
IL-21 (pg/ml)	40	22.71 [1.99-17.08]	0.04	110.75
IL-22 (ng/ml)	78	0.24 [0.04-0.04]	0.04	1.61
IL-23 (ng/ml)	13	3.46 [1.08-5.41]	0.05	10.14

n – number of observations, IQR – interquartile range, Me – median, Min. – minimum, Max. – maximum

Table 3. Spearman's rank correlations between circulating cytokines

Cytokine pair	Spearman's ρ	*p*-value	*n*
IL-21 vs. IL-22	0.51	0.001	40
IL-21 vs. IL-23†	0.82	0.004	13
IL-22 vs. IL-23†	0.70	0.011	13

ρ – Spearman's rank correlation coefficient, n – number of paired observations, bold values indicate statistically significant correlations ($p < 0.05$), † Exploratory analysis due to limited number of detectable IL-23 measurements

Obesity and the immunological mechanisms present in low-grade inflammation are interdependent. The cytokines IL-21, IL-22, and IL-23 are also interconnected. Table 3 describes the statistical correlations.

Associations between cytokines and obesity-related parameters

Due to the endocrine function of adipose tissue, the level of interleukins involved in low-grade inflammation was associated with body weight or its components. Analysis using Spearman's rank correlation showed that higher BMI values within the obese cohort were associated with lower IL-23 concentrations ($\rho = -0.62$, $p = 0.024$, $n = 13$). No significant correlations were observed between other body composition indices and cytokine levels, and the remaining correlations are shown in Supplementary Table 1.

Associations between cytokines and dietary intake and food consumption frequency (FFQ)

To examine associations between dietary intake and circulating interleukin levels, data from three-day food diaries were analyzed using nutritional analysis software to estimate average nutrient intake for each participant. Correlation analyses were then performed between dietary variables and serum cytokine concentrations. IL-22 levels were positively associated with sugar intake (Spearman's $\rho = 0.26$, $p = 0.020$), β-carotene intake ($\rho = 0.23$, $p = 0.046$), vitamin A intake ($\rho = 0.24$, $p = 0.033$), and vitamin B_2 intake ($\rho = 0.22$, $p = 0.048$). In addition, IL-23 concentrations were positively associated with fructose intake ($\rho = 0.61$, $p = 0.027$, $n = 13$). Negative associations were observed between IL-21 levels and dietary glycemic index ($\rho = -0.34$,

$p = 0.031$) as well as vitamin B_3 intake ($\rho = -0.32$, $p = 0.043$). IL-22 levels were also negatively associated with dietary glycemic index ($\rho = -0.26$, $p = 0.024$). Furthermore, IL-23 concentrations showed negative associations with dietary n-6 fatty acid intake ($\rho = -0.60$, $p = 0.030$, $n = 13$) and cholesterol intake ($\rho = -0.56$, $p = 0.047$, $n = 13$). Detailed correlation results for all analyzed nutrients are presented in Supplementary Table 2.

The FFQ-6 questionnaire was analyzed to show the influence of the frequency of consumption of individual food groups on the studied adipokines. Spearman's rank correlation analysis showed positive associations between circulating IL-22 concentrations and the frequency of consumption of sweetened carbonated beverages ($\rho = 0.24$, $p = 0.036$) and fast-food products ($\rho = 0.25$, $p = 0.025$). In addition, IL-23 levels were positively associated with the consumption of white pasta (Spearman's $\rho = 0.78$, $p = 0.002$, $n = 13$) and fast food ($\rho = 0.63$, $p = 0.020$, $n = 13$); however, these findings should be interpreted as exploratory due to the limited number of detectable IL-23 measurements. Negative associations were also observed between circulating IL-22 concentrations and the frequency of consumption of wholemeal pasta ($\rho = -0.24$, $p = 0.034$) and cottage cheese ($\rho = -0.30$, $p = 0.007$). Furthermore, IL-23 levels were negatively associated with the frequency of consumption of fish ($\rho = -0.57$, $p = 0.042$, $n = 13$), white cheese ($\rho = -0.59$, $p = 0.035$, $n = 13$), and eggs ($\rho = -0.60$, $p = 0.029$, $n = 13$); these associations should likewise be considered exploratory. Supplementary Table 3 contains a summary of the frequency of consumption of individual food groups (A) and other results of the statistical analysis (B).

Data were also obtained from a questionnaire assessing selected dietary habits and lifestyle factors, including physical activity and stimulant use. Alcohol consumption was associated with lower circulating IL-21 levels compared with non-drinkers (11.82 ±22.18 vs. 21.9 ±23). In addition, participants who reported regular physical activity exhibited higher IL-23 concentrations than physically inactive individuals (7.1 ±3 vs. 2.79 ±3.04).

Associations between cytokines and lifestyle factors and comorbidities

Additionally, exploratory analyses suggested that selected comorbidities and medications may be associated with variability in circulating interleukin levels. Participants treated for hypothyroidism ($n = 4$) exhibited higher IL-21 concentrations compared with the remaining cohort ($p = 0.018$). Isolated observations of lower IL-23 levels were noted in individual participants with non-alcoholic fatty liver disease or treated hypothyroidism.

Furthermore, single cases suggested higher IL-21 concentrations in a participant using nonsteroidal anti-inflammatory drugs occasionally and lower IL-23 levels in a participant using levothyroxine, NSAIDs, and vitamin D_3. Similarly, lower IL-21 and IL-23 levels were observed in one smoker compared with non-smokers. Due to the very small number of observations, these findings should be interpreted with caution and considered descriptive only. Further studies in larger cohorts are required to clarify the potential influence of comorbidities, medications, and smoking status on cytokine profiles.

Discussion

We observed a negative correlation between the BMI value and the level of IL-23. There are completely opposite observations in the literature. In the study by Juncal-Ruiz *et al*., among individuals with a first episode of psychosis, the concentration of this interleukin was significantly higher in overweight individuals compared to those with normal body weight. This difference was not observed in the control group of healthy individuals [16]. Among obese patients with psoriatic arthritis, weight loss over a six-month period was associated with lower circulating IL-23 levels [17]. In another study, compared to women with normal body weight, those with obesity showed higher levels of IL-23 [18]. These discrepant findings possibly suggest a context-dependent role for IL-23 in obesity-related inflammation. Although IL-23 is widely considered a proinflammatory cytokine involved in the maintenance and pathogenicity of Th17 cells, its expression and systemic availability may vary depending on disease stage, metabolic status, and tissue compartment. Furthermore, IL-23 activity may be primarily localized to tissues such as adipose tissue or the gut-associated immune system rather than being reflected in peripheral blood. Together, these mechanisms may partially explain the inverse association observed in the present study and the heterogeneity of IL-23 findings reported in different clinical and experimental settings [19-21].

In the present study, higher dietary glycemic index was associated with lower circulating levels of IL-22 and IL-21. The glycemic index is dependent on the amount of easily digestible carbohydrates, which quickly raise blood glucose levels to high values. In the study by Park *et al*., increased IL-22 levels were associated with lower blood glucose concentrations in mice fed a high-fat diet [22]. In animal models, improved glycemic control following Roux-en-Y gastric bypass surgery was associated with increased IL-22 release in the intestinal lumen [23]. High blood glucose levels among lean psoriasis patients were associated with elevated levels of IL-23 [24]. Studies assessing IL-23 levels in adipose tissue of individuals with and without obesity have demonstrated associations between IL-23 expression and metabolic inflammation as well as insulin resistance in obesity, suggesting that IL-23 may represent an interesting target for future biomarker research [25]. We also observed a positive correlation between IL-22 concentration in blood and the frequency

of consumption of sweetened beverages, high sugar intake and frequent consumption of fast food, and a negative correlation between this interleukin and the frequency of consumption of whole wheat pasta rich in fiber. Similarly, there was a positive correlation between IL-23 concentration and frequent consumption of fast food and high fructose content in the diet. The relationship between the type of diet and the concentration of the above-mentioned interleukins may be the result of changes in the profile of the intestinal microflora, as intestinal bacteria are a mediating factor in the stimulation of IL-22 and IL-23 levels. Normal gastrointestinal microflora regulates the secretion of IL-22 and IL-23 [26]. A diet low in fiber and high in fats and simple carbohydrates, characteristic of dietary patterns in highly developed countries, has been associated with alterations in gut microbiota composition, including a higher prevalence of potentially pathogenic microorganisms, and may be linked to lower circulating IL-23 levels [27]. High fiber intake has been identified in numerous studies as being associated with beneficial modulation of the gut microbiota and higher IL-22 levels [28-30]. Subjects from the study group who consumed sources of fiber such as whole wheat pasta also had elevated levels of this interleukin. In another animal study, a diet enriched in soluble fiber inulin and omega 3-PUFA suppressed IL-23 levels [31]. In the current study, higher intake of omega-6 fatty acids and cholesterol was associated with lower serum IL-23 levels in obese individuals. In contrast, Shi *et al*. reported that a Western dietary pattern, characterized by high total fat and cholesterol intake, may adversely affect gut microbiota composition and be associated with IL-23-mediated inflammatory pathways, leading to increased inflammatory responses and exacerbation of psoriatic skin and arthritis manifestations [32].

In this study, frequent consumption of cottage cheese was associated with lower levels of IL-22 and IL-23 among the study participants. It has been proven that IL-22 is involved in cow's milk protein allergy in infants [33]. In adults, this interleukin is also associated with the immune response to allergens [34]; however, allergies did not occur in the study group. Another explanation for this relationship may be the effect on probiotic bacteria used to produce cottage cheese. In the literature, there is information that bacteria of the genera *Lactobacillus*, *Lactococcus* and *Leuconostoc* can induce the production of IL-22 in B cells, because IL-22 plays a key role in the barrier functions in the intestines [35]. The relationship between the frequency of dairy consumption and IL-22 and IL-23 levels requires further research.

The positive association between β-carotene or retinol intake and circulating IL-22 concentrations may be partly related to the metabolic conversion of carotenoids into retinoic acid, a compound that has been reported to be associated with modulation of IL-22 expression [33, 36-39]. Additionally, there are no scientific reports in the literature regarding the effect of niacin on IL-21 levels and riboflavin on IL-22.

Lifestyle factors such as physical activity or stimulants also affect the functioning of the immune system, including the level of cytokines. In the present study, participants who reported regular physical activity exhibited higher circulating IL-23 levels. In contrast, Korkmaz *et al*. reported no significant effect of physical exercise on IL-23 levels in animal models [40]. To date, data on the relationship between physical activity and IL-23 levels in humans remain limited. The observed association may reflect an adaptive immune response to physical effort, analogous to exercise-related cytokine responses described for IL-6; however, this interpretation remains speculative and requires confirmation in future studies [41]. In addition, previous studies have reported increased IL-21 expression among alcohol-dependent individuals, highlighting the complex and context-dependent effects of alcohol consumption on cytokine profiles [42].

The potential anti-inflammatory effects of IL-21 and IL-23 should be considered based on negative correlations with pro-inflammatory environmental factors. Studies have shown that IL-21 balances local cytokine expression by increasing IL-10 production, decreasing TNF-α production, and regulating the production of pro-inflammatory cytokines, such as IL-17 and IL-6, by regulatory T cells (Treg) [43, 44]. Dietary ingredients such as typical components of the Western diet – saturated fatty acids, trans fatty acids, monosaccharides and disaccharides, and red meat – have a negative effect on the concentration of adiponectin. Furthermore, a diet characterized by a high glycemic index has been associated with lower circulating levels of the anti-inflammatory adiponectin [45]. Similarly, in our study, negative correlations were found between lifestyle factors and levels of IL-21, IL-22 and IL-23. The latest research confirms the pro- and anti-inflammatory effects of these interleukins depending on the tissue and the cytokine environment [46]. The anti-inflammatory effect of IL-23 may result from the interaction between IL-23 and IL-17 production, which may be a critical immune pathway, potentially regulated by the IL-12-induced interferon α (IFN-α) pathway [47]. Studies suggest that IL-12 initially drives the Th1 response and IFN-α production, but may later play an immunoregulatory role as IL-23 becomes the dominant pro-inflammatory cytokine [47, 48].

This study also confirms the interactions between IL-21, IL-22, and IL-23. IL-23 and IL-21 play an important role in the survival and expansion of Th17, which may be a factor connecting these three interleukins [49-51]. Th17 stimulates the production of IL-6 and IL-1β, and TNF-α increased the expression of IL-22 360-fold, while a high concentration of IL-23 increased the production of IL-22 up to 460-fold [50, 52].

Limitations

This study has several limitations that should be acknowledged. First, its cross-sectional design and the absence of a non-obese control group preclude causal inference and do not allow direct comparisons of cytokine levels between obese and normal-weight individuals. Therefore, the observed relationships should be interpreted as associations rather than causal effects. Second, the study population was predominantly female, which may limit the generalizability of the findings, as sex-related differences in immune responses and cytokine profiles have been reported. Third, although the age range of participants was relatively broad, the cohort consisted mainly of middle-aged adults. Age-stratified analyses were not feasible due to limited sample sizes in the youngest and oldest age groups. Another important limitation is that detectable concentrations of IL-23 were available only in a subset of participants, which may have reduced statistical power and increased susceptibility to random variation. Consequently, the findings involving IL-23 should be interpreted with caution and considered exploratory. Although participants representing obesity classes I, II, and III were included, formal comparisons between obesity classes were not performed. The study was designed to assess associations using BMI as a continuous variable, and subgroup analyses by obesity class were limited by sample size, particularly in class III obesity. Finally, dietary intake and lifestyle data were self-reported and may therefore be subject to recall bias. In addition, the inclusion of participants with obesity-related comorbidities, such as arterial hypertension and non-alcoholic fatty liver disease, may have introduced potential confounding, as these conditions are associated with systemic inflammation and can influence cytokine profiles. Nevertheless, their inclusion reflects the real-life clinical context of obesity and enhances the ecological validity of the study.

Conclusions

Within the obese cohort, higher BMI values were associated with lower circulating IL-23 concentrations, which contrasts with some previous reports. These observations do not allow conclusions regarding the effect of weight loss on IL-23 levels and should be interpreted cautiously. Physical activity was associated with higher circulating IL-23 levels, which may reflect an adaptive immune response to physical effort, similar to observations reported for exercise-induced IL-6; however, this interpretation remains speculative. Alcohol consumption was associated with lower circulating IL-21 and IL-23 levels, suggesting possible immunoregulatory associations, although existing evidence in the literature remains inconsistent. Dietary patterns were also associated with circulating cytokine levels. The intake of simple carbohydrates and dietary fiber, and frequent consumption of fast food showed associations with IL-22 and IL-23 concentrations. These relationships may be partly related to diet-associated alterations in gut microbiota; however, this hypothesis requires further investigation. In addition, the frequency of cottage cheese consumption and higher intake of omega-3 fatty acids, niacin, and riboflavin were associated with differences in the levels of the studied cytokines. Finally, the observed interrelationships between IL-21, IL-22, and IL-23 suggest coordinated regulation within obesity-related low-grade inflammation. Overall, these findings should be interpreted as exploratory and hypothesis-generating.

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Disclosures

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The authors declare no conflict of interest.

Supplementary material is available on the journal's website.

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