Exploration of micro- and macronutrient consumption and leverage of interaction with adipokines among Jordanian adults

Background and Aim: Findings related to nutrient intakes and levels of adipokines concentrations are inconclusive. The present study aimed at investigating the association between intakes of macro- and micro-nutrients with serum adipokines in apparently healthy adults.

Methods and Results: A convenient sample of 167 adults was obtained from students and employees in major hospital in Jordan. Serum concentrations of leptin, adiponectin, resistin and interleukine-6 were measured. Nutrients intakes were assessed using a validated quantitative food frequency questionnaire. Higher levels of leptin were associated with the highest consumption of energy from carbohydrate, insoluble, and soluble fiber (P=0.04). Lower levels of leptin were associated with highest consumption of energy from fat (P=0.04), monounsaturated fatty acids (P=0.04) and cholesterol (P=0.02). Lower levels of adiponectin were found among individuals with the highest consumption of carbohydrates (p=0.02) insoluble fibers (P=0.01); and copper (P=0.03). Higher levels of adiponectin were associated with higher consumption of cholesterol (P=0.03). Leptin/adiponectin ratio was positively associated with the intakes of carbohydrates (P=0.04), soluble- (P=0.01) and insoluble fibers (P=0.01) and copper (P=0.03), whereas the ratio was negatively associated with cholesterol (P=0.04), butyric acid (P=0.03) and omega-3 fatty acids (P=0.03). Levels of resistin were only associated with total fiber intake (P=0.04) and levels of interleukine-6 were only associated with cholesterol intake (P=0.01).

Conclusion: Our findings suggest that intakes of carbohydrates, fat, cholesterol and fibers are the major dietary factors that may be associated with levels of leptin and adiponectin. Levels of resistin and interleukine-6 may be less associated with diet composition.

Keywords: macronutrients, micronutrients, leptin, resistin, IL-6, adiponectin, leptin/adiponectin ratio

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Introduction

Adipose tissue is the major site for storage of excess energy in the form of triglycerides, and it contains different cell types, including mainly adipocytes, preadipocytes, endothelial cells and immune cells [1]. Adipose tissue has been recognized as an active endocrine organ secreting a variety of adipokines, which are bioactive peptides that can induce several autocrine/paracrine or endocrine effects [2]. Adipokines include cytokines e.g., tumor necrosis factor (TNF)-α, interleukins (IL-1, IL-6 and IL-10), lipid-related peptides, several enzymes, low molecular weight proteins such as leptin, adiponectin, resistin and visfatin [2-4]. Adipokines are responsible for regulating several physiological processes and functions, including food intake balance and energy homeostasis [3], insulin sensitivity [5,6], cardio and vascular protection [7,8]. For example, the protein leptin is a satiety adipokine that controls body weight by regulating appetite and energy expenditures [9-11]. Adiponectin has positive association with insulin sensitivity [12], whereas, resistin, visfatin and IL-6 have been identified as pro-inflammatory mediators, and are linked to insulin resistance and type 2 diabetes [13-15]. Obesity and adipocyte dysfunction result in a disruption of adipokine production, which may contribute to the development of obesity-linked metabolic and cardiovascular diseases via altered glucose and lipid homeostasis as well as inflammatory responses [16,17].

Several studies demonstrated a strong association between dietary intakes of several nutrients with circulating adipokine concentrations in the general population [18-20]. Some of these nutrients includeomega-3 fatty acid [21,22], protein [23], sucrose [24], and dietary [22,25], or foods such as vegetables and fruits [26], whole grain [27], fish [28,29], and legumes [30]. However, other studies showed no association between some dietary component[s] such as vitamins and minerals with adipokine levels [31-33]. Studies examined the effect of dietary intake of vitamins and minerals on serum

adipokines are scarce. Al-Daghri et al. (2012) found that increasing levels of dietary vitamin B6 and B12 have been associated with a significant increase in serum concentrations of leptin but not resistin among Saudi adults and children [34]. Levels of IL-6 and leptin were inversely associated with participants' usual dietary zinc intake and 30mg/day of zinc supplementation significantly decreased IL-6 level, whereas serum leptin and plasma adiponectin concentration did not differ with either zinc supplementation or placebo among obese women [35]. Recent observational studies showed favorable effects of the Mediterranean dietary pattern, a low-saturated fat and a high-monounsaturated fat diet, on serum adiponectin, leptin and resistin among US and Spain populations [36-38]. In contrast, high-fructose diets were associated with adverse outcomes such as low adiponectin levels and high leptin levels [39,40].

Jordan is a middle-income country located in a region of the world where dietary habits changed to western pattern considerably. Accordingly, differences and changes in dietary habits and traditional foods between populations may influence the level of those adipokines widely. To the best of our knowledge, no studies assessed the association between nutrients' intake and the following serum adipokines: leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio among healthy adults. Therefore, the present study aimed at examining the relationship between macronutrients and micronutrients intakes and serum adipokines levels in apparently healthy Jordanian adults.

Methods

Study design and participants

In this cross-sectional study, a total number of 167 (83 males and 84 females) apparently healthy Jordanian volunteers (students of Hashemite University and employees of the King Hussein Medical Center (KHMC)), aged 18-51 years were recruited conveniently during the period of October 2014 to July 2015. Sample size was calculated based on an alpha probability of 0.05 and power of 0.8. Eligibility criteria to be enrolled in the study were: being Jordanian and above 18 years old. Pregnant and lactating women and individuals with eating disorders, major surgeries or any chronic diseases were excluded from this study. A signed informed consent was obtained from each participant. The study protocol was approved by the Jordanian Royal Medical Services (JRMS) ethics committee.

Measurement of adipokines

Blood samples were drawn from participants after overnight fasting by a specialized medical laboratory technician. Serum samples were centrifuged and separated from the whole blood and stored at −80°C until further analysis. Serum inflammatory cytokine interleukine-6 (IL-6), adiponectin, resistin and leptin concentrations were measured By ELX 800 TC models 96-well Elisa Microplate Readers-USA using commercially available enzyme-linked immunosorbent assay (ELISA) kits (RayBio® Human IL-6 ELISA Kit, USA, Cat# ELH-IL-6; RayBio® Human Acrp30 ELISA Kit USA, Cat# ELH-Adiponectin; RayBio® Human Leptin ELISA Kit, USA, Cat# ELH-Leptin; RayBio® Human Resistin ELISA Kit, USA, Cat# ELH-Resistin). The reproducibility of the intra- and inter-assay coefficients of variation were <10% and <12%, respectively, for all RayBio® ELISA kits. Leptin/adiponectin ratio was calculated as leptin concentration level and divided by adiponectin concentration/level after exchanging of units.

Assessment of nutrients' intake

A validated Arabic quantitative FFQ adapted from the Diet History Questionnaire I (DHQ I) was used for dietary assessment [41]. This FFQ was used as an assessment tool to estimate nutrients consumption among our study subjects. The FFQ questions sought to obtain information on the dietary history of participants during the 12 months prior to the commencement of the study. We estimated that dietary choices during the last 12 months would be indicative of a fixed habitual pattern reflecting prior years. Participants were asked how frequently, on average, during the past year they had consumed one standard serving of specific food items in nine categories (<1/month, 2-3/month, 1-2/week, 3-4/week, 5-6/week, 1/day, 2-3/day, 4-5/day, or 6/day). Food lists in the modified FFQ questions were classified based on types of food: 21 items of fruits and juices; 21 items of vegetables; eight items of cereals; nine items of milk and dairy products; four items of beans; 16 items of meat such as red meat (lamb and beef), chicken, fish, cold meat, and others; four items of soups and sauces; five items of drinks; nine items of snacks and sweets; and 14 items of herbs and spices [41]. For better portion size estimation, food models and standard measuring tools were used.

Dietary intakes were analyzed using dietary analysis software (ESHA Food Processor SQL version 10.1.1; ESHA, Salem, OR, USA) with additional data on foods consumed in Jordan [42]. For calculating energy and nutrients intake from the food frequency questionnaire, the frequencies of food consumed were transferred into grams. Then those grams from each food item entered to the food processor program ESHA for each person participating in the study. The average for each nutrient consumed by the all participants was then calculated.

■ Statistical analysis

The data were analyzed using SPSS statistical package version 20. Energy, macronutrients and micronutrients were presented as mean ± standard error. Leptin, resistin, IL-6, adiponectin, leptin/adiponectin ratio were grouped into tertiles. Tertiles were generated using the SPSS statistical program in which the program defines tertile as 33 and 66 percentiles of the nutrients consumed. Therefore, T1 represents less than 33, T2 between 33-66, and T3 above 66 percentiles of the amount of nutrients consumed by the study participants. Post-hoc Analysis of Variance (ANOVA) was used to assess the impact of energy, macronutrients and micronutrients intake on serum adipokines after adjustment for age, sex, BMI, energy intake, physical activity and smoking. Different letters denotes significant differences among the tertiles. P-values<0.05 were considered statistically significant.

Results

Participants' demographic and anthropometric data, the concentration / level of leptin, resistin, IL-6, and adiponectin were published previously in another publication [43]. The authors reported significant statistical differences (P<0.01) between normal body weight, overweight and obese participants in serum leptin, resistin, IL-6 and adiponectin. The serum levels of leptin, resistin and IL-6 were significantly (P<0.01) greater in obese participants than those levels reported for overweight and normal body weight participants. Adiponectin serum concentrations were significantly lower in obese participants compared to overweight and normal body weight participants.

The association between participants' daily total energy intake and macronutrients' contribution to energy intake in relation to their serum adipokines and IL-6 is presented in **TABLE 1**. Leptin was significantly associated with the highest consumption of energy from carbohydrate among participants in the highest tertile (P=0.04). On the contrary, participants in the highest tertiles of adiponectin had the lowest consumption of energy from carbohydrate (P=0.03). Leptin was significantly associated with the highest energy intake from fat among participants in the lowest and middle tertiles (P=0.04). There was no significant association between total energy and protein consumption across different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio. Furthermore, there was no statistically significant relationship with total energy and macronutrient distribution consumptions across all tertiles for resistin and IL-6.

TABLE 2 shows participants' daily intake of different macronutrients through different tertiles of serum adipokines and IL-6. Higher levels of leptin were significantly associated with the higher intake of insoluble fiber (P=0.01), where lower levels of leptin were associated with the higher intake of monounsaturated fatty acids (P=0.04) and cholesterol (P=0.02). Only one significant difference was observed between the daily intakes of different macronutrients across all tertiles of resistin and IL-6. Participants in the lowest and highest tertiles of resistin had the highest intake of fiber compared to participants in the middle tertile (P=0.04). Lower levels of IL-6 were significantly associated with an increased consumption of cholesterol compared to higher level (P=0.01). Adiponectin was positively associated with cholesterol (P=0.03) and negatively with total carbohydrate (P=0.02) and insoluble fiber (P=0.01). The consumption of total carbohydrate (P=0.04), soluble fiber (P=0.01), and insoluble fiber (P=0.01) were positively associated with leptin/adiponectin ratio. Conversely, the leptin/adiponectin ratio was negatively associated with cholesterol (P=0.04), butyric fatty acid (P=0.03) and omega-3 fatty acids (P=0.04). Participants in the highest tertile of the adiponectin had significantly the lowest intake of copper when compared to participants in the lowest tertile (P=0.03). The higher leptin/adiponectin ratio was associated with an increased level of copper consumption compared to the lower ratio, where the difference reached a conventional level for statistical significance (P=0.03). There was no statistically significant association with other fat soluble and water soluble vitamins as well as calcium, iron and zinc intake through all tertiles of the analyzed serum adipokines **(TABLE 3).**

Table 1. Percentages of energy intakes and distribution across different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio.

Nutrients	T (n)	Leptin		Resistin		IL6		Adiponectin		Leptin/Adiponectin ratio	
		Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value
Total Energy (kcal)	T1 (45)	2756.4 ± 143.0	0.34	2852.4 ± 187.5	0.79	3100.9 ± 165.9	0.56	3198.8 ± 176.5	0.21	2738.9 ± 144.0	0.10
	T2 (46)	2966.7 ±200.1		3015.1 ± 174.8		2889.4 ± 176.7		2834.5 ± 179.2		2859.6 ± 193.5	
	T3 (45)	3117.3 ± 171.2		2971.8 ± 160.3		2851.8 ± 179.2		2810.1 ± 162.0		3244.3 ± 173.5	
Percent energy from carbohydrates	T1 (45)	612 ± 1.3[a]	0.04	63.53 ± 1.23	0.26	61.0 ± 1.3	0.07	65.1 ± 1.4[b]	0.03	61.6 ± 1.2	0.07
	T2 (46)	61.8 ± 1.3[a]		61.10 ± 1.46		62.3 ± 1.2		63.2 ± 1.2[ab]		61.6 ± 1.2	
	T3 (45)	65.6 ± 1.3[b]		63.93 ± 1.22		65.3 ± 1.4		60.2 ± 1.2[a]		65.3 ± 1.5	
Percent energy from fats	T1 (45)	29.6 ± 1.1[b]	0.04	27.97 ± 1.02	0.13	29.6 ± 1.1	0.07	27.3 ± 1.2	0.10	29.3 ± 1.0	0.18
	T2 (46)	29.6 ± 1.0[b]		30.19 ± 1.12		29.4 ± 1.1		27.8 ± 0.9		29.3 ± 0.9	
	T3 (45)	26.3 ± 1.0[a]		27.31 ± 1.04		26.5 ± 0.9		30.4 ± 1.1		26.9 ± 1.2	
Percent energy from proteins	T1 (45)	12.5 ± 0.4	0.41	11.99 ± 0.35	0.93	12.5 ± 0.3	0.41	11.4 ± 0.3	0.07	12.4 ± 0.4	0.31
	T2 (46)	11.99 ± 0.3		12.19 ± 0.44		11.8 ± 0.4		12.3 ± 0.4		12.2 ± 0.4	
	T3 (45)	11.8 ± 0.3		12.09 ± 0.29		12.1 ± 0.3		12.5 ± 0.4		11.6 ± 0.3	

Statistical significant difference (P<0.05)
Different letters denotes significant differences among the tertiles.
T stands for Tertile.
The leptin/adiponectin ratio was calculated as leptin concentration level and divided by adiponectin concentration/level.

Table 2. Mean ± SEM for adjusted macronutrients intake in different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio.

Nutrients	T (n)	Leptin		Resistin		IL-6		Adiponectin		Leptin/Adiponectin ratio	
		Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value	Mean ± SEM	*P*-value
Total Carbohydrate. g	T1 (45)	509.0 ± 12.3	0.07	528.5 ± 13.1	0.54	508.2 ± 12.1	0.17	549.7 ± 15.5^{b}	0.02	511.1 ± 12.0^{a}	0.04
	T2 (46)	511.5 ± 13.2		510.9 ±15.1		517.6 ± 11.9		520.9 ± 10.8^{ab}		507.2 ± 10-.9^{a}	
	T3 (45)	547.8 ± 13.5		529.0 ± 10.9		542.4 ± 15.0		497.5 ± 12.0^{a}		550.1 ± 15.6^{b}	
Starch. g	T1 (45)	2.0 ± 0.5	0.66	2.4 ± 0.5	0.25	1.8 ± 0.5	0.96	1.9 ± 0.5	0.85	2.0 ± 0.5	0.80
	T2 (46)	1.5 ± 0.3		1.6 ± 0.4		1.9 ± 0.4		1.6 ± 0.3		1.6 ±0.3	
	T3 (45)	2.0 ± 0.5		1.5 ± 0.3		1.8 ± 0.4		1.9 ± 0.5		1.9 ± 0.5	
Fiber. g	T1 (45)	56.9 ± 2.0	0.46	60.6 ± 2.2^{b}	0.04	57.5 ± 2.5	0.64	61.3 ± 2.2	0.18	57.3 ± 2.0	0.17
	T2 (46)	57.5 ± 2.1		54.0 ± 2.1^{a}		57.5 ± 2.2		57.7 ± 2.0		56.1 ± 2.1	
	T3 (45)	60.4 ± 2.2		60.3 ± 1.9^{b}		59.9 ± 1.7		55.8 ± 2.1		61.5 ± 2.2	
Soluble Fiber. g	T1 (45)	6.4 ± 0.6^{a}	0.04	6.6 ± 0.6	0.26	7.3 ± 0.6	0.11	8.5 ± 0.7	0.08	6.7 ± 0.6^{a}	0.01
	T2 (46)	7.2 ± 0.6^{ab}		7.7 ± 0.7		6.6 ± 0.7		7.3 ± 0.6		6.7 ± 0.6^{a}	
	T3 (45)	8.7 ± 0.7^{b}		8.0 ± 0.6		8.5 ± 0.6		6.5 ± 0.62		8.9 ± 0.6^{b}	
Insoluble Fiber. g	T1 (45)	10.8 ± 0.8^{a}	0.01	12.20 ± 1.0	0.37	12.6 ± 1.0	0.27	15.0 ± 1.1^{b}	0.01	11.1 ± 0.9^{a}	0.00
	T2 (46)	12.1± 1.0^{a}		12.1 ± 0.9		11.7 ± 1.0		12.3 ± 0.9^{a}		11.5 ± 0.9^{a}	
	T3 (45)	15.3 ± 1.1^{b}		13.9 ± 1.1		13.9 ± 1.0		10.8 ± 0.9^{a}		15.6 ± 1.1^{b}	
Oligosaccharide. g	T1 (45)	264.1 ± 7.7	0.84	262.8 ± 8.7	0.79	259.9 ± 8.7	0.59	267.3 ± 7.9	0.97	268.1 ± 7.3	0.61
	T2 (46)	265.4 ± 7.7		270.5 ± 7.7		269.5 ± 7.5		265.1 ± 8.5		260.5 ± 8.7	
	T3 (45)	270.4 ± 8.6		266.5 ± 7.5		270.4 ± 7.7		267.6 ± 6.2		271.4 ± 7.9	
Protein. g	T1 (45)	101.0 ± 3.0	0.41	97.4 ± 2.6	0.93	102.4 ± 2.7	0.15	94.1 ± 2.3	0.14	100.5 ± 3.0	0.53
	T2 (46)	96.9 ± 2.4		97.9 ± 3.3		95.4 ± 2.9		98.4 ± 2.7		97.4 ±2.5	
	T3 (45)	96.4 ± 2.7		98.9 ± 2.1		96.5 ± 2.4		101.7 ± 3.0		96.4 ± 2.6	
Fat. g	T1 (45)	116.3 ± 4.7	0.06	110.3 ± 5.1	0.37	115.5 ± 4.6	0.26	104.2 ± 5.6	0.06	115.7 ± 4.6	0.05
	T2 (46)	117.7 ± 4.7		117.9 ± 5.0		115.8 ± 4.6		112.6 ± 3.9		118.5 ± 4.0	
	T3 (45)	103.2 ± 4.9		109.0 ± 4.3		105.9 ± 5.1		120.4 ± 4.6		102.9 ± 5.5	
Saturated Fat. g	T1 (45)	33.1± 1.5	0.17	31.7 ± 1.6	0.10	36.8 ± 2.7	0.06	30.0 ± 1.9	0.06	33.3 ± 1.5	0.12
	T2 (46)	35.8 ± 2.6		36.5 ± 2.5		32.5 ± 1.5		32.9 ± 1.5		35.9 ± 2.2	
	T3 (45)	30.5 ± 1.6		31.2 ± 1.5		30.2 ± 1.4		36.6 ± 2.3		30.1 ± 2.1	

Table 2. Mean ± SEM for adjusted macronutrients intake in different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio.

Monounsaturated Fat. g	T1 (45)	28.4 ± 1.5[b]	0.04	27.4 ± 1.7	0.87	24.8 ± 1.6	0.22	25.4 ± 1.8	0.63	28.5 ± 1.5	0.15
	T2 (46)	28.3 ± 1.8[b]		26.3 ± 1.9		28.8 ± 1.8		26.8 ± 1.4		27.4 ± 1.6	
	T3 (45)	23.3 ± 1.5[a]		26.3 ±1.4		26.3 ± 1.5		27.7 ± 1.7		24.1 ± 1.8	
Polyunsaturated Fat. g	T1 (45)	23.5 ± 1.7	0.24	22.3 ± 1.9	0.75	19.1 ± 1.6	0.09	19.9 ± 1.8	0.39	23.5 ± 1.7	0.22
	T2 (46)	21.6 ± 1.9		20.5 ± 1.7		24.4 ± 1.9		21.1 ± 1.6		21.6 ± 1.6	
	T3 (45)	19.3 ± 1.6		21.6 ± 1.7		20.9 ± 1.5		23.3 ± 1.8		19.3 ± 1.8	
Trans Fat. g	T1 (45)	3.2 ± 0.5	0.42	3.5 ± 0.5	0.42	2.9 ± 0.4	0.59	3.2 ± 0.4	0.77	3.2 ± 0.5	0.82
	T2 (46)	3.6 ± 0.3		3.4 ± 0.4		3.5 ± 0.5		3.5 ± 0.4		3.4 ± 0.4	
	T3 (45)	2.9 ± 0.4		2.8 ± 0.3		3.2 ± 0.4		3.0 ± 0.5		3.1 ± 0.4	
Cholesterol. mg	T1 (45)	259.3 ± 28.1[b]	0.02	204.8 ± 14.3	0.71	270.5 ± 28.7[b]	0.01	174.7 ± 12.3[a]	0.02	251.3 ± 27.9[b]	0.04
	T2 (46)	190.4 ± 15.5[a]		227.0 ± 39.2		188.4 ± 13.6[a]		211.6 ± 17.2[ab]		210.6 ± 17.0[ab]	
	T3 (45)	190.6 ± 14.3[a]		207.5 ± 14.6		181.4 ± 13.8[a]		253.5 ± 28.1[b]		177.8 ± 13.1[a]	
Butyric Fatty Acid	T1 (45)	0.1 ± 0.01	0.45	0.1 ± 0.0	0.62	0.1 ± 0.0	0.43	0.1 ± 0.0	0.25	0.1 ± 0.01[b]	0.03
	T2 (46)	0.1 ±0.01		0.1 ± 0.0		0.1 ± 0.0		0.1 ± 0.0		0.1 ± 0.01[ab]	
	T3 (45)	0.1 ± 0.01		0.1 ± 0.0		0.1 ± 0.0		0.1 ± 0.0		0.1 ± 0.01[a]	
Omega-6 Fatty Acids. g	T1 (45)	20.8 ± 1.7	0.13	19.6 ± 1.9	0.70	15.9 ± 1.7	0.06	16.5 ± 1.9	0.27	21.3 ± 1.8	0.11
	T2 (46)	19.3 ± 2.1		17.5 ± 1.9		21.9 ± 2.0		18.7 ± 1.6		18.6 ± 1.7	
	T3 (45)	15.8 ± 1.6		18.8 ± 1.6		18.1 ± 1.7		20.7 ± 1.9		15.9 ± 1.9	
Omega-3Fatty Acids. g	T1 (45)	1.6 ± 0.1	0.08	1.5 ± 0.2	0.64	1.20 ± 0.14	0.14	1.2 ± 0.2	0.13	1.7 ± 0.1[b]	0.04
	T2 (46)	1.5 ± 0.2		1.3 ± 0.2		1.62 ± 0.16		1.4 ± 0.1		1.4 ± 0.2[ab]	
	T3 (45)	1.2 ± 0.1		1.4 ± 0.1		1.38 ± 0.14		1.6 ± 0.2		1.1 ± 0.2[a]	

Statistical significant difference (P< 0.05)
Different letters denotes significant differences among the tertiles.
T stands for Tertile.
The leptin/adiponectin ratio was calculated as leptin concentration level and divided by adiponectin concentration/level.

Table 3. Mean ± SEM for adjusted micronutrients intake across different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio.

Nutrients	T (n)	Leptin		Resistin		IL6		Adiponectin		Leptin/Adiponectin ratio	
		Mean ± SEM	*p*-value	Mean ± SEM	*p*-value	Mean ± SEM	*p*-value	Mean ± SEM	*p*-value	Mean ± SEM	*p*-value
Vitamin A. IU	T1 (45)	18967.5 ± 1976.3	0.53	20332.4 ± 2007.1	0.89	19633.2 ± 1892.9	0.99	20482.8 ± 2344.8	0.55	18548.4 ± 1938.8	0.78
	T2 (46)	21764.8 ± 2723.0		18941.7 ± 2476.2		19890.4 ± 2566.5		21001.5 ± 2265.9		20125.6 ± 2291.6	
	T3 (45)	18558.9 ± 1741.3		20079.8 ± 2089.5		19808.8 ± 2088.1		17823.9 ± 1957.4		20653.6 ± 2350.8	
Vitamin A. RE	T1 (45)	2367.2 ± 213.1	0.52	2476.3 ± 212.5	0.80	2419.1 ± 190.7	0.96	2390.3 ± 236.6	0.66	2293.2 ± 206.9	0.91
	T2 (46)	2556.3 ± 267.4		2265.2 ± 249.5		2372.5 ± 262.9		2508.9 ± 228.0		2424.9 ± 232.3	
	T3 (45)	2193.1 ± 183.8		2381.7 ± 211.6		2329.1 ± 216.3		2218.4 ± 210.1		2401.5 ± 236.8	
β carotene. mg	T1 (45)	7858.6 ± 1014.3	0.37	8664.1 ± 1055.7	0.99	8229.5 ± 985.1	0.90	9301.7 ± 1330.9	0.47	7802.9 ± 1011.9	0.64
	T2 (46)	10042.1 ± 1558.2		8744.6 ± 1453.4		8964.6 ± 1425.2		9240.3 ± 1243.2		8761.1 ±1258.7	
	T3 (45)	8066.5 ± 930.2		8587.4 ± 1084.5		8797.1 ± 1182.7		7443.2 ± 1030.4		9431.7 ± 1337.5	
Vitamin D. mg	T1 (45)	1.2 ± 0.3	0.23	1.0 ± 0.3	0.71	1.0 ± 0.2	0.63	0.7 ± 0.2	0.28	1.19 ± 0.3	0.20
	T2 (46)	0.6 ± 0.2		0.8 ± 0.2		0.9 ± 0.3		0.7 ± 0.2		0.68 ± 0.2	
	T3 (45)	0.8 ± 0.2		0.7 ± 0.2		0.7 ± 0.2		1.2 ±0.3		0.68 ± 0.2	
Vitamin E. mg	T1 (45)	18.9 ± 4.3	0.51	19.6 ± 4.8	0.34	13.6 ± 1.5	0.49	14.09 ± 2.5	0.66	18.98 ± 4.3	0.48
	T2 (46)	14.5 ± 2.4		13.4 ± 1.4		18.8 ± 4.5		15.32 ± 2.6		14.77 ± 2.4	
	T3 (45)	14.2 ± 2.5		14.5 ± 2.4		15.08 ± 2.7		18.12 ± 4.2		13.80 ± 2.5	
Vitamin K. mg	T1 (45)	167.2 ± 33.1	0.50	185.0 ± 31.5	0.76	178.3 ± 29.1	0.32	223.9 ± 40.1	0.41	176.2 ± 33. 9	0.71
	T2 (46)	248.4 ± 67.1		235.5 ± 68.6		268.2 ± 72.0		244.3 ± 65.8		231.5 ± 65.2	
	T3 (45)	209.3 ± 37.2		204.7 ± 36.2		178.1 ± 29.4		156.8 ± 32.1		217.6 ± 40.4	
Folate.mg	T1 (45)	587.5 ± 130.2	0.50	622.5 ± 141.1	0.27	451.0 ± 42.6	0.69	447.7 ± 71.3	0.68	589.3 ± 130.2	0.49
	T2 (46)	453.9 ± 68.8		431.6 ± 41.9		560.6 ± 136.1		483.3 ± 73.9		458.9 ± 68.9	
	T3 (45)	452.9 ± 71.5		440.7 ± 70.7		480.2 ± 77.2		562.6 ± 127.8		445.9 ± 71.3	
Vit.B12. mg	T1 (45)	9.1 ±1.9	0.17	9.1 ±2.1	0.17	6.5 ± 0.8	0.69	5.4 ±1.1	0.28	9.0 ± 1.9	0.16
	T2 (46)	6.0 ± 1.1		5.6 ± 0.8		7.9 ± 2.0		6.7 ± 1.2		6.4 ± 1.1	
	T3 (45)	5.6 ± 1.1		6.0 ± 1.0		6.3 ± 1.2		8.6 ± 1.9		5.2 ± 1.1	
Vit.C. mg	T1 (45)	270.5 ± 39. 7	0.73	359.7 ± 51.0	0.13	292.7 ± 41.9	0.59	344.1 ± 47.9	0.27	266.4 ± 39.5	0.49
	T2 (46)	298.8 ± 46.6		238.3 ± 41.5		266.9 ± 40.3		297.7 ± 43.6		284.9 ± 40.4	
	T3 (45)	318.5 ± 42.4		291.2 ± 33.2		328.9 ± 46.6		246.1 ± 35.7		336.9 ± 48.4	
Calcium. mg	T1 (45)	1653.1 ± 341.7	0.54	1792.5 ± 367.0	0.21	1359.3 ± 125.2	0.78	1304.1 ± 215.0	0.65	1661.6 ± 340.9	0.58
	T2 (46)	1253.0 ± 180.8		1164.8 ± 113.3		1589.3 ± 355.9		1393.4 ± 200.3		1344.8 ± 187.6	
	T3 (45)	1426.0 ± 219.3		1376.8 ± 219.3		1376.1 ± 227.9		1631.5 ± 333.7		1323.6 ± 214.9	
Copper. mg	T1 (45)	1.3 ± 0.1	0.26	1.4 ± 0.1	0.61	1.4 ± 0.1	0.88	1.6 ± 0.1 [a]	0.03	1.3 ± 0.1[a]	0.03
	T2 (46)	1.5 ± 0.1		1.5 ± 0.1		1.4 ± 0.1		1.4 ± 0.1[ab]		1.4 ± 0.1[ab]	
	T3 (45)	1.5 ± 0.1		1.5 ± 0.1		1.5 ± 0.1		1.3 ± 0.1 [b]		1.6 ± 0.1[b]	

Table 3. Mean ± SEM for adjusted micronutrients intake across different tertiles of leptin, resistin, IL-6, adiponectin and leptin/adiponectin ratio.

Iron. mg	T1 (45)	36.0 ± 6.0	0.41	36.9 ± 6.4	0.26	29.4 ± 1.9	0.77	28.8 ± 3.1	0.56	36.1 ± 5.9	0.39
	T2 (46)	28.6 ± 3.0		27.5 ± 1.0		33.7 ± 6.2		30.2 ± 3.4		28.6 ± 3.1	
	T3 (45)	29.4 ± 3.1		29.6 ± 3.0		30.8 ± 3.3		34.9 ± 5.8		29.2 ± 3.1	
Zinc. mg	T1 (45)	23.1 ± 4.7	0.32	23.5 ± 5.2	0.25	16.4 ± 1.6	0.53	16.1 ± 2.6	0.42	23.4 ± 4.7	0.27
	T2 (46)	16.9 ± 2.7		15.9 ± 1.7		21.8 ± 5.0		17.9 ± 2.9		16.9 ± 2.7	
	T3 (45)	16.4 ± 2.6		17.1 ± 2.5		18.1 ± 2.8		22.4 ± 4.6		16.0 ± 2.6	

Statistical significant difference (P<0.05)
Different letters denotes significant differences among the tertiles.
Abbreviations: Retinol Equivalent, RE; International Unit, IU; Tertiles, T.
The leptin/adiponectin ratio was calculated as leptin concentration level and divided by adiponectin concentration/level.

Discussion

Dietary components may modulate the risk of diseases by altering the levels of adipokines secretion and/or sensitivity [33,44,45]. In this study of Jordanian adults, we highlighted a few associations between dietary consumption of macro- and micro-nutrients and serum levels of leptin, adiponectin, IL-6, resistin, as well as leptin/adiponectin ratio.

The consumption of carbohydrate plays an integral role in the regulation of leptin level and adiponectin due to the concurrent changes in glucose homeostasis and insulin secretion [44,46]. Adiponectin/leptin ratio may provide a reliable measure of insulin sensitivity [47]. A high carbohydrate diet promotes glucose intolerance and insulin secretion as well as reduces insulin sensitivity, therefore, increases leptin, an insulin-resistance surrogate, and reduces adiponectin, an insulin sensitivity surrogate [46,48,49]. A higher consumption of carbohydrate has been found to augment leptin level [44], which is in agreement with the positive association between serum leptin level and energy percent from carbohydrates that has been detected in this study. In contrast, circulating adiponectin concentration was negatively associated with glycemic load and glycemic index [20]. Also, an increased consumption of total carbohydrate has been found to be associated with a reduced level of circulating adiponectin [18,20,50], which supports our finding of a higher carbohydrate consumption (percent of energy from carbohydrate and amount of carbohydrate) among the lowest tertile of serum adiponectin.

In contrast to other studies, this study found positive associations between leptin and leptin/adiponectin levels and fiber consumption (soluble and insoluble) as well as a negative association between insoluble fiber and adiponectin. Additionally, the middle tertile of serum resistin was found to be associated with the lowest fiber consumption compared to the lowest and highest tertiles. An increased fiber consumption is associated with an enhanced dietary carbohydrate quality, and consequently with better glycemic control and insulin sensitivity [50]. Additionally, fiber consumption has been previously reported to be associated with an increased level of adiponectin and a decreased level of leptin [44,50-53]. Elevated fiber intake may play a protective role against systemic inflammation [52], but the evidence regarding the association between fiber consumption and resistin is still controversial. One dietary fiber-derivative, propionic acid, was found to inhibit the expression level of resistin, a component of inflammation and insulin resistance [54]. The consumption of a healthy dietary pattern was associated with a significant reduction in resistin level in a large sample of apparently healthy women and the researchers suggested that the effect was mediated, partly, by cereal fiber consumption [35]. However, Parikh et al. (2012) reported a lack of association between resistin level and fiber consumption [52]. To the best of our knowledge, higher fiber consumption generally enhances the sensitivity of insulin and leptin, reduces the circulating concentration of leptin, and increases the circulating adiponectin level. Therefore, it is hard to give a convincing explanation for the detected associations between fiber consumption and levels of adipokines, these associations would highlight the diet complexity and the importance of overall diet quality, where a high fiber intake does not necessarily mean healthier choices or better diet quality.

The consumption of a high amount of dietary fat elevates the circulating leptin level and eventually reduces the cellular responsiveness to leptin [27,55]. Unlike saturated fatty acid, monounsaturated and polyunsaturated fatty acids were found to reduce the circulating concentrations of leptin [44]. Results from the present study identified negative associations between serum leptin level and the percent energy from fat as well as the amount of monounsaturated fatty acid consumed. The association between fat consumption and leptin concentration is provocative; with results indicating a positive [56,57], negative [58], and no association [59]. This might be due to the variation in participants' characteristics, study design, dietary fat quality, or overall diet quality. While most of the available evidence assessed the effect of polyunsaturated and saturated fatty acid on circulating leptin levels [60-62], little is known about the effect of monounsaturated fatty acid. However, the Mediterranean diet, monounsaturated fat-rich diet, was found to reduce leptin level. Dietary monounsaturated fat was found to significantly reduce serum leptin compared to saturated fatty acid and carbohydrate [63], which might be, partly, explained by the beneficial effect of the consumption of monounsaturated fatty acid on insulin sensitivity [63,64]. Further research is warranted to evaluate the effect of monounsaturated fatty acid consumption on leptin levels.

In this study, higher cholesterol consumption was found to be associated with a higher level of adiponectin and lower levels of leptin, IL-6, and leptin/adiponectin ratio. Cholesterol synthesis and absorption have been found to be associated with serum levels of several adipokines including leptin and adiponectin [65]. The association between serum levels of adipokines and cholesterol metabolism challenges the explanation of the association between cholesterol consumption and serum levels of these adipokines. Also, the cholesterol consumption of the participant in this study was within the normal range (<300 mg/dL) which further challenges the interpretation of these association.

Regarding the detected association between butyric acid and leptin/adiponectin ratio, it was not possible to find any association between dietary butyric acid and adiponectin or leptin during the present study. However, short-chain fatty acids have been found to improve glycemic control, modulate nutrient trafficking and oxidation, modulate the expression level of several proteins/enzymes, that regulate energy balance including leptin, and may positively affect body weight control [54,66,67]. Given the involvement of leptin and adiponectin in glucose and energy metabolism, the negative association between butyric acid consumption and leptin/adiponectin ratio that has been detected in the current study, may reflect the beneficial metabolic effect of butyric acid. More studies are needed to support this association.

Participants in the highest tertile of leptin/adiponectin ratio had a significantly lower intake of omega-3 fatty acid compared to those in the lowest tertile. Omega-3 fatty acid was previously reported to modulate the levels of adiponectin, leptin and adiponectin/leptin ratio. Serum adiponectin levels significantly increased following 8-week of 3 g/d of omega-3 fatty acid supplementation in healthy young female [29]. Also, an increased dietary consumption of fish was found to be associated with a reduced level of leptin [28]. Mostowik et al. (2013) found that daily supplementation of 1 g/d of omega-3 fatty acid for 30 days significantly increased adiponectin level and adiponectin/leptin ratio as well as resulted in a significant reduction in leptin level [68]. The effect of omega-3 fatty acid on adiponectin and leptin levels is suggested to be a concomitant to its modulatory effects on cytokine and proinflammatory mediators [21].

Data concerning the association between adipokine levels and copper consumption is scarce, however, copper and adiponectin are involved in several similar metabolic processes including oxidative defense system and glycemic control, in which the levels of adiponectin and copper were negatively, associated with the risk factors of abnormal health conditions such as diabetes, cardiovascular disease, and oxidative stress [69-71]. Additionally, copper has been suggested as a possible mediator of leptin levels regulation [72]. A positive association between serum level of leptin and serum level of copper, a surrogate marker of its consumption, has been reported in healthy adult as well as in female athletes [72,73]. Therefore, findings of this study might reflect a possible role of copper in the regulation of circulating level of adiponectin. Further research is warranted to test the possible modulatory effect of copper consumption on serum adiponectin levels.

One of the strong points of this study is the use of a validated Arabic FFQ that was modified to reflect the food consumption pattern in Arab countries, especially Jordan. Furthermore, the strength of this study can be attributed to the use of food models and measurements tools to help the participants to estimate portion sizes. The main limitation of this study, however, is the one year dietary recall period, which may be affected by behavioral and dietary changes, memory and bias. Cross-sectional study design cannot assess the cause and effect relationship between nutrients and adipokines level. In addition, our sample size is small due to the limited financial support for the biochemical analyses. Therefore, we recommend conducting additional studies to detect the effect not just the association between nutrients intake and the level of serum adipokines. Additionally, another study on a large-scale is warranted to generalize these findings.

In conclusion, the results of the present study highlighted that the consumption of some nutrients (carbohydrates, fibers, fats, monounsaturated fats, cholesterol and copper) may ameliorate the circulating adipokines in different aspects.

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Conflict of interests

The authors declare that they have no conflict of interests.

Authority

RFT NSH and AMA participated in conception and design of the study. NAN, LMA and SSA entered data and performed biochemical analysis and statistical analysis. RFT, NSH, BAB, SH, and AMA interpreted the study results and drafted the manuscript.

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