The Association of Dietary Acid Load with Resting Metabolic Rate and Metabolic Components in Overweight and Obese Women: A Cross Sectional Study

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Research note

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Abstract

Objective: Several epidemiologic studies have reported that dietary acid load is associated with metabolic profiles; however, to our knowledge, the relationship of this dietary pattern with resting metabolic rate (RMR) among obese and overweight females remains unreported. Therefore, this study aimed to evaluate the association of dietary acid load RMR and metabolic components among overweight and obese adult women.

Results: It was observed that after correction for potential confounders, DBP and NEAP and **PRAL** scores were inversely associated ($P < 0.05$). NEAP index was inversely associated with RMR ($\beta = -0.25$, 95% CI = -0.1.5 to 2.08, $P = 0.02$), and positively associated with WC ($\beta = 1.009$, 95% CI = -1.43 to 3.45, $P = 0.05$) and WHR ($\beta = 0.01$, 95% CI = -0.01 to 0.04, $P = 0.03$), such that subjects with higher scores in NEAP had lower RMR and higher WC and WHR. We also observed that DAL ($\beta = -0.02$, 95% CI = -0.08 to 0.03, $P = 0.08$) and PRAL ($\beta = -0.037$, 95% CI = -1.05 to 0.03 $P = 0.07$) were marginally associated with RMR.

Introduction

The prevalence of obesity are increasing globally, it has been demonstrated that obesity is strongly related to several life-limiting disorders, including cardiovascular diseases and diabetes (1). Obesity is regarded as a may be influenced by eating habits, low energy expenditure(2).

The role of acid–base homeostasis in cardio-metabolic risk factors has recently been posited (3, 4). Animal protein such as fish and meat are influential in a higher acid production in the body while, vegetables and fruits are known as alkaline foods (5, 6). Dietary patterns have evolved towards a western-style diet, which is defined by a higher intake of animal products, fast foods that result in higher production of acid in body (4, 7).

Potential renal acid load (PRAL), net endogenous acid production (NEAP) (8), and dietary acid load (DAL) (9) indexes are commonly used to estimate dietary acid load in epidemiological studies. PRAL and DAL scores are, generally, better predictors of dietary acid load, as, in those formulas, calcium, phosphorus, and magnesium, as well as protein and potassium, are included; while NEAP is calculated, simply, by the ratio of protein and potassium (5, 10). Accordingly, a negative PRAL value demonstrates a base forming potential, while a positive value indicates an acid-forming potential (11).

Previous studies have mainly focused on the association of acid/base imbalance on kidney stones and bone health (12, 13) metabolic syndrome (14). Metabolic acidosis, which can be influenced by dietary factors (15–17), may adversely affect blood pressure (18–20) through an increase in cortisol production (15, 21, 22). Higher production of cortisol, as the result of metabolic acidosis (15, 17), may also have an adverse influence on the other cardio-metabolic risk factors, including hypertension, hypocholesteremia and insulin resistance (IR) (23, 24). Indeed, several studies have illustrated that resting metabolic rate (RMR) can be reduced in type 2 diabetes with IR (25). It has been posited that individuals with low RMR are at higher risk of developing obesity-related disorders(26).

In the present study, we assessed the relationship between three score of dietary acid load and metabolic components and RMR in overweight and obese women.

Materials And Methods

Study population

In the current study 375 women aged 18 to 48, with a body mass index (BMI) ≥ 25 kg/m², were recruited from Health Centers in Tehran, Iran between 2017–2019. The Medical Research Ethics Committee of Tehran University of Medical Sciences (TUMS) approved the study with the following identification IR.TUMS.VCR.REC.1395.1597. All participants expressed their willingness to participate in the study by providing informed written consent. The overall exclusion criteria were as follows: any history of acute and chronic disease including hypertension, diabetes mellitus, cardiovascular disease, and impaired renal and liver function, as well as regular use of medicine, pregnant or lactating, intake of alcohol, smoking, and menopause. In addition, participants who had been following any arbitrary special dietary regimen, as well as those with chronic disease(s) affecting their diet, or if their daily energy intake was < 800 kcal or > 4200 kcal (27), were excluded.

Dietary assessment

Dietary intake was assessed using a validated semi quantitative food frequency questionnaire (FFQ) with 147- food items(28). All FFQs were completed by a trained dietitian, who asked participants to designate their intake frequency for each food item consumed during the past year, on a daily, weekly, or monthly basis. Finally, we converted portion sizes of foods to grams by using household measures (29).

Assessment of dietary acid load

Dietary acid-base load was evaluated via 3 indexes: PRAL, NEAP, and DAL which were calculated by using nutrients derived from the FFQ with the following formulas:

1. PRAL (mEq/d) = $0.4888 \times \text{dietary protein (g/d)} + 0.0366 \times \text{dietary phosphorus (mg/d)} - 0.0205 \times \text{dietary potassium (mg/d)} - 0.0125 \times \text{calcium (mg/d)} - 0.0263 \times \text{magnesium (mg/d)}$ (30)
2. NEAP = $54.5 \times \text{dietary protein (g/d)} / \text{dietary potassium (mg/d)} - 10.2$ (31)
3. DAL (mEq/ day) = PRAL + (body surface area (m²) $\times 41$ (mEq / day)/1.73 m²) (32)

Body surface area (BSA) was calculated using the Du Bois formula: $0.007184 \times \text{height } 0.725 \times \text{weight } 0.425$ (9, 33). We adjusted both PRAL and NEAP for total energy intake, employing the residual method.

Anthropometric assessments

Weight was determined on a digital scale, where participants wore light indoor clothing, without shoes, and was recorded to the nearest 100 g. Height was measured to the nearest 0.5 cm while participants were in the normal standing position, without shoes. Waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) were measured according to standard procedures(34).

Blood pressure assessment

Blood pressure measurements were taken using a standard mercury sphygmomanometer.

Physical activity

The Short form of the International Physical Activity Questionnaire (IPAQ) (35) was applied to evaluate physical activity and according to the frequency and time of common activities of daily life over the past year (36).

Measurement of biochemical parameters

Fasting serum glucose, insulin, total cholesterol, triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) were measured from blood samples drawn after 8–12 h of overnight fasting. All samples were assessed by standard methods at the Nutrition and Biochemistry Laboratory of the school of Nutritional and Dietetics at TUMS. IR was estimated by homeostasis model assessment (HOMA)(37)

Resting metabolic rate assessment

RMR measurement was performed by professional nutritionists using a standard protocol (38), and was measured by indirect calorimetry (spirometer METALYZERR 3B-R3, Cortex Biophysik GmbH, Leipzig, Germany).

Complete body composition analysis

Body composition of subjects was evaluated via Body Composition Analyzer BC-418MA- In Body (United Kingdom), in accordance with manufacturer guidelines.

Statistical analysis

The Kolmogorov–Smirnov test was used to assess the distribution of the data. Baseline characteristics of participants were compared by independent samples t test between the median of PRAL, NEAP, and DAL score and chi square(χ^2) tests for categorical variables. Also, we adjusted variables for confounders using Analysis of covariance (ANCOVA). General linear regression (GLM) was used to assess the association of scores with body composition, biochemical variables and RMR per kg. Data were analyzed using IBM SPSS version 25.0(SPSS, Chicago, IL, USA) and P-values ≤ 0.05 were considered for significant.

Result

Study Population Characteristics

The mean of quantitative variables including; age, BMI, RMR, of the participants in our study were; 36.67 years (SD = 9.1), 30.98 kg/m² (SD = 3.9), 1574.96 kg/day (SD = 259.71).

Association between quantitative and qualitative variables among acid load scores

Physical activity was higher in high intake of PRAL, NEAP, DAL and also about age in high intake of NEAP ($P < 0.05$). FFM was higher in high intake of PRAL and DAL ($P < 0.05$) and normal RMR was higher in low intake of NEAP ($P = 0.04$) (Table 1).

Table 1
Study participant characteristics between High and Low acid load scores

Variables	PRAL		P-value	P-value†	NEAP		P-value	P-value†	DAL		P-value	P-value†	
	Low	High			Low	High			Low	High			
	(<-19.98)	(≥-19.98)			(<-9.03)	(≥-9.03)			(<-18.52)	(≥-18.52)			
Age (years)	35.77 ± 8.78	37.17 ± 9.25	0.14	0.29	35.44 ± 8.78	37.36 ± 9.22	0.04	0.11	35.58 ± 8.71	37.24 ± 9.26	0.08	0.11	
Physical activity (MET-minutes/week)	854.07 ± 919.3	1560.98 ± 2782.47	<0.001	0.02	88.83 ± 944.30	1538.56 ± 2789.83	0.01	0.04	863.00 ± 930.01	1530.74 ± 2745.44	<0.001	0.02	
Anthropometric variables													
Weight(kg)	79.64 ± 10.36	80.64 ± 11.43	0.13	0.30	79.60 ± 10.46	80.66 ± 11.37	0.36	0.78	79.64 ± 10.36	80.64 ± 11.43	0.38	0.36	
Height(cm)	161.49 ± 6.08	161.06 ± 5.74	0.38	0.02	161.53 ± 6.10	161.04 ± 5.74	0.42	0.21	161.43 ± 6.04	161.10 ± 5.78	0.97	0.02	
HC(cm)	105.66 ± 6.05	105.65 ± 9.16	0.99	0.83	105.65 ± 6.10	105.66 ± 9.14	0.98	0.56	105.35 ± 5.71	105.82 ± 9.2	0.87	0.56	
BMI (kg/m²)	Crude	30.70 ± 3.89	0.28	0.22	30.66 ± 3.86	30.16 ± 3.91	0.22	0.30	30.64 ± 3.84	31.17 ± 3.92	0.19	0.11	
	Model 1	30.84 ± 0.31			30.29 ± 0.32	30.88 ± 0.31			30.33 ± 0.32	30.79 ± 0.31			30.28 ± 0.31
Body composition													
BFM(kg)	Crude	34.30 ± 8.40	0.45	0.13	34.14 ± 8.46	35.08 ± 9.87	0.30	0.56	33.55 ± 7.44	35.37 ± 9.33	0.04	0.11	
	Model 1	33.79 ± 0.26			33.63 ± 0.27	34.23±0.45			33.19 ± 32.97	33.78 ± 0.26			33.26 ± 0.27
FFM(kg)	Crude	46.51 ± 5.49	0.98	0.01	46.65 ± 5.61	46.45 ± 5.78	0.74	0.47	46.17 ± 5.21	45.71 ± 5.96	0.37	0.01	
	Model 1	46.12 ± 0.46			47.02 ± 0.47	46.33 ± 0.45			46.81 ± 0.47	46.10 ± 0.46			47.04 ± 0.47
Deviation from normal RMR	Crude	-7.65 ± 13.09	0.27	0.06	-7.57 ± 12.03	-9.32 ± 12.03	0.23	0.04	-7.72 ± 13.09	-9.14 ± 0.96	0.33	0.11	
	Model1 ^{II}	-7.40 ± 1.18			-9.14 ± 1.23	-7.37 ± 1.12			-10.09 ± 1.15	-7.49 ± 1.12			-9.98 ± 1.17
Qualitative variables													
Economic status			0.42	0.31			0.46	0.69			0.34	0.11	
Low level		34(38.6)	54(61.4)		32(36.4)		56(63.6)		33(37.5)		55(62.5)		
Moderate level		72(39.1)	112(60.9)		72(39.1)		112(60.9)		70(38)		114(62)		
High level		35(31.8)	75(68.2)		35(31.8)		75(68.2)		33(30)		77(70)		
Education level												0.73	0.11
Illiterate		25(1)	3(75)		0.84	0.48	1(25)	3(75)	0.74	0.68	1(25)	3(75)	
Under diploma		17(34.7)	32(65.3)				16(32.7)	33(67.3)			16(32.7)	33(67.3)	
Diploma		54(35.3)	99 (64.7)				54(35.3)	99(64.7)			51(33.3)	102(66.7)	
Master and higher		73(38.6)	116(61.4)				74(39.2)	115(60.8)			72(38.1)	117(61.9)	
Marital status			0.40	0.69			0.10	0.17			0.29	0.11	
Single		35)32.1 (	74)67.9 (		33(30.3)		76(69.7)		34(31.2)		75(68.8)		
Married		110)38.5 (	176)61.5 (		112(39.2)		174(60.8)		106(37.1)		180(62.9)		

Variables	PRAL		P-value	P-value [†]	NEAP		P-value	P-value [†]	DAL		P-value	P-value [†]
	Low	High			Low	High			Low	High		
	(<-19.98)	(≥-19.98)			(<-9.03)	(≥-9.03)			(<-18.52)	(≥-18.52)		
HC, Hip circumference; BMI, body mass index, BFM, body fat mass; FFM, fat free mass; PRAL, potential renal acid load; DAL, dietary acid load NEAP, net endogenous acid production												
Values are mean ±SD for crude model and mean± SE for adjusted model and qualitative variables are presented as n (%).												
All variables adjusted with age, energy intake, physical activity, BMI, economic status												
Model1 : further adjustment for fat free mass												
Crude P-value obtained from independent sample T test.												
† adjust P-value obtained from analysis of covariance												

Association between some dietary intake components among acid load scores

After adjustment for confounders, cereals consumption was higher in high intake of all three scores (PRAL, NEAP, DAL) and fruits consumption was higher in low intake of all three scores (P < 0.001); vegetables consumption was higher in low PRAL and DAL scores, and fat intake was higher in high PRAL, NEAP, and DAL scores (Table 2).

Table 2
Dietary intakes of study population between high and low acid load Scores

Variables	PRAL		P-value [†]	NEAP		P-value [†]	DAL		P-value [†]
	Low (<-19.98)	High (≥-19.98)		Low (<-9.03)	High (≥-9.03)		Low (<-18.52)	High (≥-18.52)	
Food groups									
Cereal(g/d)	1258.95 ± 16.39	1357.70 ± 16.87	< 0.001	1256.23 ± 16.23	1361.47 ± 16.89	< 0.001	1258.95 ± 16.39	1357.70 ± 16.87	< 0.001
Fruits(g/d)	1676.69 ± 22.31	652.15 ± 23.89	< 0.001	1668.69 ± 22.42	1395.42 ± 23.28	< 0.001	1677.69 ± 22.31	1390.6 ± 22.78	< 0.001
Vegetables(g/d)	497.74 ± 2012	294.69 ± 19.59	< 0.001	305.59 ± 19.84	487 ± 20.55	< 0.001	1215.59 ± 19.79	1013 ± 20.15	< 0.001
Legumes(g/d)	263.40 ± 3.78	261.41 ± 3.88	0.52	264.23 ± 3.57	260.49 ± 3.70	0.47	263.30 ± 3.60	261.52 ± 3.68	0.73
Nuts(g/d)	144.98 ± 1.37	138.81 ± 1.41	<0.001	144.09 ± 1.38	139.72 ± 1.43	0.03	145.30 ± 11.18	138.53 ± 18.59	<0.001
Dairy(g/d)	1272.09 ± 21.60	1234.64 ± 21.32	0.26	1272.09 ± 20.66	1244.64 ± 21.37	0.36	1260.49 ± 20.90	1257.09 ± 22.02	0.97
Eggs(g/d)	19.77 ± 1.28	23.94 ± 1.31	0.02	19.11 ± 1.26	24.68 ± 19.11	0.003	19.92 ± 1.29	23.74 ± 1.31	0.04
Meat [*] (g/d)	350.42.39 ± 4.53	366.12 ± 4.66	0.01	349.40 ± 4.66	367.36 ± 4.66	0.007	351.43 ± 4.57	364.95 ± 4.66	0.04
Energy and macronutrients									
Energy (kcal)	2515.59 ± 66.65	2703.51.45	0.02	2530.33 ± 66.75	2694.62 ± 51.52	0.05	2491.56 ± 67.66	2713.20 ± 50.81	<0.001
Carbohydrates(g/d)	370.85 ± 42.57	330.47 ± 46.58	< 0.001	369.86 ± 3.81	331.67 ± 3.96	< 0.001	370.77 ± 3.83	331.37 ± 3.91	< 0.001
Fat (g/d)	99.93 ± 0.51	112.69 ± 0.39	< 0.001	100.55 ± 1.71	112.12 ± 1.77	< 0.001	99.86 ± 0.53	112.65 ± 0.39	< 0.001
protein (g/d)	92.00 ± 0.21	93.28 ± 0.16	0.56	91.40 ± 0.21	93.94 ± 0.16	0.25	92.00 ± 0.21	93.28 ± 0.16	0.13
Total fiber(g/d)	44.32 ± 1.35	49.40 ± 1.04	0.05	43.83 ± 1.22	47.13 ± 1.23	0.06	44.100 ± 1.25	46.76 ± 1.22	0.13
MUFA(g/d)	33.98 ± 0.71	30.87 ± 0.55	< 0.001	33.72 ± 0.72	29.20 ± 0.73	< 0.001	33.25 ± 0.75	29.82 ± 0.73	0.001
PUFA(g/d)	30.87 ± 0.55	21.87 ± 0.62	<0.001	21.58 ± 0.64	18.60 ± 0.64	<0.001	21.18 ± 0.66	19.09 ± 0.64	0.02
SFA(g/d)	27.51 ± 0.47	29.97 ± 0.61	< 0.001	29.69 ± 0.63	26.87 ± 0.64	<0.001	30.09 ± 0.64	26.60 ± 0.63	< 0.001
Micronutrients and caffeine									
Iron (mg/d)	18.88 ± 1.52	31.30 ± 1.17	0.09	18.60 ± 0.24	18.82 ± 0.25	0.53	18.48 ± 0.25	18.93 ± 0.24	0.20
Zinc (mg/d)	12.70 ± 0.21	13.84 ± 0.16	0.08	12.74 ± 0.19	13.11 ± 0.19	0.17	12.71 ± 0.19	13.13 ± 0.19	0.13
Calcium (mg/d)	1151.11 ± 32.71	1339.63 ± 25.29	0.19	1234.98 ± 25.38	1205.600 ± 25.66	0.05	1153.14 ± 26.10	1185.86 ± 25.44	0.37
Magnesium(mg/d)	504.41 ± 6.14	428 ± 7.96	< 0.001	490.45 ± 6.84	428.44 ± 6.77	< 0.001	489.47 ± 6.75	427.19 ± 6.93	< 0.001
Potassium (mEq/d)	4931.33 ± 63.14	2499.4 ± 209.9	< 0.001	4993.33 ± 67.53	3690.11 ± 66.79	< 0.001	4959.74 ± 67.68	3677.52 ± 69.43	< 0.001
Sodium (mg/d)	4347.68 ± 108.48	4852.55	0.18	4360.44 ± 98.48	4679.05 ± 102.48	0.02	4353.21 ± 9.16	4681.28 ± 101.69	0.02
Phosphor (mg/d)	1633.98 ± 25.98	1700.7 ± 20.07	0.68	1624.61 ± 25.42	1658.69 ± 25.70	0.35	1637.81 ± 26.04	1644.95 ± 25.38	0.84
Vitamin C(mg/d)	216.63 ± 6.19	141.18 ± 8.01	< 0.001	250.43v8.38	145.16 ± 8.29	< 0.001	250.17 ± 8.2	141.57 ± 8.43	< 0.001
Vitamin E(mg/d)	18.38 ± 0.68	16.23 ± 0.52	0.24	18.36 ± 0.73	16.51 ± 0.74	0.08	17.85 ± 0.75	17.05 ± 0.74	0.45
Vitamin A (mg/d)	887.79 ± 30.03	673.3 ± 29.70	< 0.001	888.46 ± 29.94	672.71 ± 29.61	< 0.001	879.99 ± 29.67	673.67 ± 29.67	< 0.001
Thiamin (mg/d)	2.18 ± 0.04	2.12 ± 0.03	0.001	2.00 ± 0.03	2.18 ± 0.2	< 0.001	2.22 ± 0.02	2.17 ± 0.03	< 0.001

Variables	PRAL		P-value [†]	NEAP		P-value [†]	DAL		P-value [†]
	Low (<-19.98)	High (≥-19.98)		Low (<-9.03)	High (≥-9.03)		Low (<-18.52)	High (≥-18.52)	
Riboflavin (mg/d)	2.18 ± 0.04	2.33 ± 0.03	0.44	2.17 ± 0.04	2.25 ± 0.04	0.23	2.19 ± 0.04	2.22 ± 0.04	0.64
Niacin (mg/d)	38.59 ± 0.52	39.54 ± 0.40	0.94	38.33 ± 0.50	40.21 ± 0.51	0.01	38.67 ± 0.52	39.83 ± 0.51	0.14
Vitamin B6(mg/d)	2.04 ± 0.03	2.29 ± 0.02	< 0.001	2.07 ± 0.03	2.27 ± 0.03	< 0.001	2.04 ± 0.03	2.29 ± 0.03	< 0.001
Folate (mcg/d)	648.23 ± 9.10	612.54 ± 7.03	<0.001	643.00 ± 8.98	617.42 ± 8.99	0.06	648.71 ± 9.06	612.39 ± 8.83	0.01
Vitamin B12(mcg/d)	13.50 ± 0.18	14.00 ± 0.14	0.06	13.50 ± 0.18	14.01 ± 0.18	0.05	13.52 ± 0.18	13.98 ± 0.17	0.09
Caffeine (mg/d)	162.93 ± 16.07	315.66 ± 53.44	<0.001	161.72 ± 13.52	205.25 ± 14.10	0.02	163.14 ± 13.67	203.03 ± 14.02	0.04
MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; PRAL, potential renal acid load; DAL, dietary acid load NEAP, net endogenous acid production Values are mean ±SE. Nutrients and food groups were adjusted for age, BMI, physical activity and total energy intake. ^: Meat alternatives included meat, poultry and sea foods. † adjust P-value obtained from analysis of covariance.									

Relationship of body composition, blood parameters, RMR and acid load scores

We observed a positive association for NEAP with WC (P = 0.05), WHR (P = 0.03), TG (P = 0.01), also, hs-CRP was positively associated with DAL score (P ≤ 0.05). A negative association between NEAP and RMR per kg was found (β= -0.66, 95% CI=-1.37 to -0.04, P = 0.05) in crude model, and in the final model this association became stronger (β= -0.25, 95%CI= -0.1.5 to 2.08, P = 0.02), and a marginal negative association for PRAL (β= -0.03, 95% CI= -1.05 to 0.03, P = 0.07) and DAL (β= -0.02, 95% CI=-0.08 to 0.03, P = 0.08) was found (Table 3).

Table 3
Association between body composition, blood parameters and all RMR per kg(kcal/d) between high and low acid load scores

Variables		PRAL		P-value	P-value*	NEAP		P-value	P-value*	DAL		P-value
		β	CI (95%)			β	CI (95%)			β	CI (95%)	
Body composition												
WC(cm)	Crude	0.28	-1.66,2.22	0.77	-	-1.71	-4.12,0.69	0.16	-	-0.03	-0.08,0.1	0.19
	Model 1	-0.02	-0.04,0.004	-	0.10	-1.09	-3.39,1.21	-	0.35	-1.04	-3.40,1.31	-
	Model 2	0.04	-1.31,0.04	-	0.33	1.009	-1.43,3.45	-	0.05	-0.05	-0.13,0.02	-
NC(cm)	Crude	-1.26	-3.26,0.73	0.21		-1.12	-4.23,1.20	0.18	-	-1.20	-2.61,0.92	-
	Model 1	-0.03	-0.09,0.03	-	0.34	-1.35	-4.68,1.96	-	0.42	-1.49	-3.91,0.93	-
	Model 2	-0.17	-0.40,0.05	-	0.13	-5.95	-13.46,1.56	-	0.12	-0.14	-0.36,0.08	-
WHR	Crude	-1.07	-0.03,0.03	0.98	-	-0.13	-1.51,1.23	0.84	-	0.00	-0.032,0.03	0.99
	Model 1	0.00	1.001,0.000	-	0.03	-0.00	-0.02,0.00	-	0.17	-0.008	-0.02,0.00	-
	Model 2	0.001	-0.001,0.01	-	0.72	0.01	-0.01,0.04	-	0.03	0.001	-0.001,-0.00	-
WHtR	Crude	0.004	-0.008,0.01	0.24	-	-0.01	-0.02,0.003	0.11	-	0.001	0.00-0.004	0.29
	Model 1	0.00	0.001-0.00	-	0.09	-0.007	-0.02,0.007	-	0.29	-0.008	-0.02,0.00	-
	Model 2	0.00	-0.001,0.00	-	0.60	0.002	-0.01,0.01	-	0.72	0.001	-0.001,0.00	-
Biochemical variables												
FBS (mg/dL)	Crude	0.04	-0.02,0.1	0.19	-	2.84	0.29,5.38	0.02	-	0.03	-0.02,0.09	0.24
	Model 1	0.06	-0.004,0.12	-	0.05	2.89	0.27,5.51	-	0.03	0.06	-0.003,0.12	-
	Model 2	0.92	0.08,1.76	-	0.03	3.82	-1.96,9.60	-	0.01	0.93	0.10, 1.76	-
Insulin (mIU/ ml)	Crude	0.001	-0.001,0.002	0.41	-	0.02	-0.03,0.087	0.40	-	0.001	-0.001,0.002	0.58
	Model 1	0.001	-0.02,0.00	-	0.24	0.01	-0.05,0.04	-	0.51	0.01	-0.05,1.01	-
	Model 2	0.004	-0.01,0.00	-	0.07	0.01	0.00,0.16	-	0.09	0.001	-0.006,0.001	-
HOMA-IR	Crude	0.004	-0.004,0.01	0.28	-	0.21	-0.12,0.56	0.21	-	0.004	-0.004,0.01	0.29
	Model 1	0.007	-0.006,0.03	-	0.17	0.19	-0.14,0.52	-	0.26	0.007	-0.001,0.016	-
	Model 2	0.046	-0.06,0.15	-	0.02	0.13	-0.90,0.64	-	0.09	0.043	-0.06,0.15	-
Total cholesterol(mg/dL)	Crude	3.69	-5.13,12.51	0.41	-	2.47	-7.20,12.15	0.61	-	0.08	-0.13,0.31	0.44
	Model 1	0.003	-0.24,0.24	-	0.98	0.86	-8.89,10.61	-	0.17	0.56	-9.02,10.15	-
	Model 2	0.69	-1.51,0.13	-	0.10	2.086	-24.98,20.81	-	0.85	-0.59	-1.34,0.15	-
TG(mg/dL)	Crude	0.12	-0.24,0.50	0.50	-	6.18	-9.77,22.13	0.76	-	0.13	-0.23,0.49	0.48
	Model 1	0.004	-0.42,0.43	-	0.98	4.11	-12.93,21.16	-	0.04	-9.61	-26.48,7.25	-
	Model 2	-0.093	-1.58,1.40	-	0.90	26.96	-14.05,67.99	-	0.01	0.09	-1.23,1.42	-
HDL (mg/dL)	Crude	-2.26	-4.93,0.40	0.09	-	-1.67	-4.56,1.21	0.25	-	-0.029	-0.09,0.04	0.40
	Model 1	-0.03	-0.10,0.04	-	0.42	-1.34	-4.35,1.65	-	0.37	-1.060	-4.67,1.47	-
	Model 2	-0.02	-0.28,0.23	-	-0.20	-1.32	-8.48,5.82	-	0.71	-0.04	-0.28,0.19	-
LDL (mg/dL)	Crude	1.28	-0.62,3.19	0.18	-	-2.62	-9.07,3.82	0.42	-	0.009	-0.14,0.16	0.90
	Model 1	-0.01	-0.17,0.15	-	0.88	-1.67	-8.14,4.78	-	0.60	-0.01	-6.53,6.50	-
	Model 2	0.136	-7.00,0.42	-	0.63	-6.73	-22.25,8.78	-	0.39	0.08	-0.42,0.59	-
Hs-CRP(mg/l)	Crude	-0.88	-2.05,0.27	0.13	-	-1.10	-2.35,0.13	0.08	-	-0.02	-0.05,0.00	0.13
	Model 1	0.01	-0.04,0.01	-	0.36	-0.94	-2.30,0.41	-	0.17	0.72	2.03,0.57	-
	Model 2	1.08	-0.22,1.10	-	0.06	2.76	-5.93,0.41	-	0.08	0.11	-0.21, 0.16	-
SBP (mmHg)	Crude	-0.02	-0.10,0.06	0.60	-	-1.46	-5.03,2.09	0.41	-	-0.02	-0.10,0.05	0.59

Variables		PRAL		P-value	P-value*	NEAP		P-value	P-value*	DAL		P-value
		β	CI (95%)			β	CI (95%)			β	CI (95%)	
	Model 1	-0.05	-0.14,0.03	-	0.19	-2.00	-5.60,1.60	-	0.27	-0.05	-0.14,0.02	-
	Model 2	-0.11	-0.42,0.19	-	0.47	0.29	-7.75,8.35	-	0.94	-0.05	-0.33,0.23	-
	Crude	-0.03	-0.09,0.01	0.17	-	-2.07	-4.56,0.41	0.10	-	-0.03	-0.09,0.01	0.18
DBP (mmHg)	Model 1	0.04	-0.11,0.06	-	0.12	1.12	-4.71,1.22	-	0.09	0.01	-0.10,-0.11	-
	Model 2	0.33	-0.47,-1.15	-	0.04	0.64	-4.99,6.28	-	0.02	0.37	-0.42,1.18	-
	Crude	-0.57	-1.27,0.13	0.11	-	-0.66	-1.37,0.04	0.05	-	-0.009	-0.02,0.00	0.34
RMR per kg (kcal/day)	Model 1	-0.135	-0.96,0.69	-	0.74	-0.28	-1.109,0.53	-	0.08	-0.31	-1.13,0.50	-
	Model2[#]	-0.338	-1.118-0.442	-	0.39	-0.44	-1.21,-0.32	-	0.04	-0.33	-1.11,0.44	-
	Model3^{&}	-0.037	-1.05,0.03	-	0.07	-0.25	-0.1,5,2.08	-	0.02	-0.02	-0.08,0.03	-

HC, Hip circumference; WC, Waist circumference; NC, neck circumference; WHtR, Waist to height ratio; WHR, Waist to hip ratio; HDL, high density lipoprotein-cholesterol; LDL, low density lipoprotein-cholesterol; TG, Triglycerides; FBS, Fasting blood sugar; HOMA, Homeostatic model assessment, RMR, Resting metabolic rate, BSA, Body surface area; resting metabolic rate; PRAL, potential renal acid load; DAL, dietary acid load NEAP, net endogenous acid production, SBP, Systolic blood pressure; DBP, Diastolic blood pressure; AST, Aspartate Aminotransferase, ALT, Alanine Transferase, Hs-CRP, high-sensitivity C-reactive protein, RQ, respiratory quotient

Values are mean $\pm$ SD for crude model and mean $\pm$ SE for adjusted model.

Model 1: Adjusted for: age, BMI, physical activity, total energy intake, economic status

Model 2: Additionally controlled for significant dietary intakes in Table 2. For PRAL, we controlled the effect cereal, fruits, vegetables, nuts, egg, meat, carbohydrate total fat intake, phosphorus, total fiber, MUFA, PUFA, SFA, caffeine and some of micronutrients magnesium, potassium, vitamin C, A, B1, B6, B9 and B12, NEAP we controlled for calcium, sodium, B3 apart from iron. For Dal score we controlled for all confounder for NEAP apart from B12.

Model2[#]: Adjusted for: age, BMI, physical activity and total energy intake and fat free mass

Model3[&]: Model2[#] confounder variables additionally controlled for significant dietary intakes in Table 2. For PRAL, we controlled the effect cereal, fruits, vegetables, nuts, egg, meat, carbohydrate, total fat intake, phosphorus, total fiber, MUFA, PUFA, SFA, caffeine and some of micronutrients magnesium, potassium, vitamin C, A, B1, B6, B9 and B12, NEAP we controlled for calcium, sodium, B3 apart from iron. For Dal score we controlled for all confounder for NEAP apart from B12.

Crude p-value for all variables obtained from independent sample T test.

*P-value obtained from adjustment. All of p-values obtained from analysis of General linear model.

Definition of RMR per kg:

Discussion

The results of this study showed a significant association between NEAP intake and RMR, TG. In addition, a favorable relationship was observed between HOMA-IR and PRAL, as well as DAL

Diet acid load scores have been predicted and validated in people with kidney diseases (39), however, to date, studies have reported conflicting findings regarding the relationship of dietary acid load and cardio-metabolic risk factors (11, 14, 39–41). Indeed, several studies suggested that higher acid load has a negative association (14, 39, 40), while others refuted this association (11, 39).

The current study showed a significant association of NEAP and PRAL with DBP. Studies have reported that in metabolic acidosis related to diet, blood pressure was increased (18, 20). The Nurses' Health Study II, which was conducted on 1136 women, showed that a higher NEAP is connected with a greater risk of hypertension (39). However, this relationship is not universally supported; for instance, it has been reported that no association between blood pressure and dietary acid load was evident among participants that were higher than 55 years old (11). Confounding the equivocal reports, the mechanism underlying the proposed relationship have not been well defined, although several pathways have been suggested, such as reduction in elimination of citrate, higher production of cortisol, and higher excretion of calcium (15, 21, 42).

The association of glycemic profile and dietary acid load has been investigated in several studies. In the present study, we showed that subjects with higher dietary acid score had greater HOMA-IR. It was reported that all of metabolic acidosis markers, such as low serum bicarbonate, higher anion gap, and low urine pH are associated with insulin resistance (14, 43) Sakhaee, et al suggested that subjects with a lower urinary pH had greater prevalence of glucose intolerance and type 2 diabetes in comparison with normal counterparts (12). Several studies have reported that an acidogenic diet may contribute to IR by constantly inducing a chronic acidosis condition in body (44, 45). It is also proposed that insulin tendency to bind to its receptors is lessened in metabolic acidosis, which results in IR, albeit in animal studies (46). Moreover, insulin discharge is reduced whenever the body is faced with acid/base variations (47). Another possible mechanism may be related to the association of greater dietary acid load with higher discharge of magnesium, which decreases insulin sensitivity (48).

The associations of urinary acidosis with biochemical parameters have been evaluated in several studies, yet, in spite of controversial results among such studies, we showed a positive association with dietary acid load and TG, WC, and WHR, and a negative relationship with RMR among the subjects. The

influence of an acidogenic diet on RMR can be the result of higher IR (45). In a cohort of 782 adults, reported that RMR and IR were significantly related (49), thus, it can be inferred that higher acid load, by increasing the IR, may reduce RMR. This finding may be suggested as an effective impact of a diet with a lower acid load in women with higher than normal BMI (39). Berg et al did not report any meaningful correlation between urinary acidosis and TG, HDL, and HbA1c(4).

The association of the dietary acid load and metabolic factors has not been fully discerned, therefore, the underlying mechanisms of how an acidogenic diet influences metabolic outcomes have not been well explained. As mentioned above, animal protein in the diet may represent a cause of increasing acid load in body. The current study focused on overweight and obese women. In addition, the validation of dietary acid load measurement methods among obese and overweight subjects is important; it has been shown that higher protein intake is not the only cause of higher acid production (50). Indeed, in the present study, we also observed that higher consumption of cereals, sodium, fat, and energy intake is related to higher acid load (50).

Conclusion

We found that dietary acid load scores were significantly related to lower RMR and higher WC, WHR, DBP and HOMA-IR in overweight and obese women.

Limitation

The present study was conducted on only one gender, so cannot be extrapolated to males. The number of participants were relatively low, moreover, based on the cross-sectional design of the study, we are not able to show any causal inference. Another limitation for assessing dietary intakes from FFQ is misclassification. Albeit we controlled for the effect of the potential confounder by the statistical methods, because of unknown confounder cannot be excluded residual confounding will affect.

Abbreviations

ARIC

Atherosclerosis Risk in Communities, **B**:beta, **BIA**:Bioelectrical Impedance Analyzer, **BMI**:Body mass index, **BIA**:Bioelectrical impedance analysis, **BSA**:Body surface area, **BW**:body weight, **BFM**:body fat mass, **CIs**:con-fidence intervals, **CVD**:cardiovascular disease, **DAL**:dietary acid load, **DBP**:diastolic blood pressure, **FBS**:fasting blood sugar, **FFM**:Fat Free Mass, **GLM**:General linear regression, **HbA1C**:Hemoglobin A1C, **HC**:hip circumferences, **HDL**:High density lipoprotein cholesterol, **HOMA-IR**:Homeostatic model assessment insulin resistance, **hs-CRP**:Hypersensitive C - reactive protein, **IR**:insulin resistance, **IPAQ**:International Physical Activity Questionnaire, **LDL**:Low density lipoprotein cholesterol, **PRAL**:potential renal acidload, **NC**:Neck circumference, **NEAP**:net endogenous acid production, **SDs**:Standard Deviations, **SEs**:standard Errors, **TC**:total cholesterol, **TG**:Triglyceride, **TUMS**:Tehran university of medical science, **WC**:Waist circumference, **WHR**:waist and hip, **WtHtR**:waist-to-height ratio

Declarations

Ethics approval and consent to participate

The study protocol has approved by the ethics committee of Tehran University of Medical Sciences (TUMS) with the following identification: IR.TUMS.VCR.REC.1395.1597. All methods were carried out in accordance with relevant guidelines and regulations. Each participant was completely informed about the study protocol and provided a written and informed consent form before taking part in the study

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from Khadijeh Mirzaei but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Khadijeh Mirzaei.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

The project was designed and implemented by AM and KhM. Data were analyzed and interpreted FSH. LS, AM, AT and CC prepared the manuscript. KhM, supervised overall project.

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