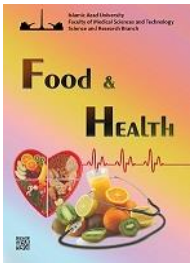

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The association of dietary acid load with metabolic syndrome: A cross-sectional study

Pegah Rahbarinejad[1], Ariyo Movahedi[1*]

[1] Department of Nutrition, Science and Research Branch, Islamic Azad University, Tehran, Iran

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ABSTRACT

Acid-base status, which can be affected by dietary acid load, has been related to risk factors for metabolic syndrome (MetS). In the current study, we investigated the association between dietary acid load and metabolic syndrome among children and adolescents. This cross-sectional study was conducted on 500 participants, aged 8-18 years old. The dietary intake of participants was assessed using a validated semi-quantitative food frequency questionnaire, and the potential renal acid load (PRAL) and net endogenous acid production (NEAP) scores were calculated. Multiple logistic regression models were used to estimate the risk of metabolic syndrome according to the PRAL and NEAP quartile categories. The mean age of the participants was 12.9±2.5 years old. Mean PRAL and NEAP scores were -4.23 and -19.70 mEq/day, respectively. In this study, the potential confounders including age, sex, BMI, and total energy, were adjusted in the multivariable-adjusted model. By using logistic regression, no significant association was observed between PEAL and NEAP with metabolic syndrome (OR= 0.98, 95% CI: 0.55-1.55, p-value=0.775 and OR=0.88, 95% CI: 0.49-1.39, p-value=0.418, respectively), after adjustment for potential confounders. Longitudinal studies should be conducted to evaluate the association between PRAL and NEAP with metabolic syndrome in children.

1. Introduction

Metabolic syndrome (MetS) is nowadays a public health challenge worldwide. In addition, MetS is a serious health condition that affects both adults and children. The prevalence and magnitude of childhood obesity are increasing dramatically, which induces a higher prevalence of metabolic syndrome among this aged group (1). Metabolic syndrome (MetS) is characterized by a cluster of central obesity, high blood pressure, high serum triglyceride levels, low serum high-density lipoprotein (HDL) cholesterol levels, and high fasting blood sugar (FBS), with insulin resistance. The underlying causes of metabolic syndrome include physical inactivity, genetic factors, getting older, unhealthy diets, overweight, and obesity (2). Besides of all modifiable and non-modifiable health determinants, diet is one of the most important determinants which can ameliorate or deteriorate chronic conditions (3, 4). Adherence to healthy dietary patterns can play a key role in preventing some chronic diseases including CVDs and MetS (3, 4). Since investigating individual foods and food components may not demonstrate the overall acid-base potential of the diet, measuring the dietary acid load (DAL) is one approach that has been frequently used for dietary acid-base evaluation in epidemiological studies (5-7). Potential renal acid load (PRAL) and net endogenous acid production (NEAP) are two scores that provide an estimation of acid-base load from dietary intake information (8). The PRAL score is based on dietary intakes of protein, potassium, calcium, magnesium, and phosphorous (8, 9). NEAP is calculated using total protein and potassium, which are the crucial determinants of metabolic acidosis (10). Both scores have been validated against objective measures of acid-base load determined from 24-h urine in healthy adults (9, 10). Based on both formula of Remer and Manz and the formula of Frasetto, the median value for the Western dietary pattern was higher than the vegan pattern (9-12). Higher consumption of animal products and processed should be compensated by higher consumption of fruits and vegetables due to reducing metabolic acidosis (13). As animal products contain a higher value of protein and

*Corresponding author: Department of Nutrition, Science and Research Branch, Islamic Azad University, Tehran, Iran.
E-mail address: amm35@mail.aub.edu (Ariyo Movahedi).

potassium, they lead to produce more potential inorganic and endogenous acid (13). However, alkaline foods such as fruit and vegetable encompass higher magnesium and potassium content which can neutralize acid-derived food intake (14, 15). The literature suggests that the achievements of ideal acid-alkaline balance can prevent metabolic acidosis. However, the lack of acid-alkaline balance may lead to stimulate cortisol production, which can be related to MetS and other chronic conditions (13, 16). To our knowledge, there is limited literature on the association between DAL with risk factors of CVDs and MetS. As the progression of Mets and CVD begins from childhood (17), it is important to evaluate the relation between DAL and Mets among children and adolescents. To date, no study has examined the association between DAL and MetS among adults. Therefore, the aim of the current study was to evaluate the association of DAL with MetS among children and adolescents.

2. Material and methods

2.1. Participants

This cross-sectional study was conducted on 500 children and adolescents, aged 8-18 years. Individuals were eligible for inclusion if they had no known medical illnesses such as diabetes, kidney, liver disease, and cardiovascular diseases (based on physician examination and medical records review), and were not taking any pharmaceutical agents.

2.2. Dietary assessment and definition of DAL

A valid and reliable semi-quantitative food frequency questionnaire (FFQ) was used to collect dietary intakes. In the current study, trained nutritionists asked children to designate their consumption frequency for each food item consumed during the previous year, on a daily, weekly, or monthly basis. Energy and nutrient contents of food items were analyzed using the USDA Food Composition Table (FCT), and for traditional Iranian foods that were not provided by the USDA FCT, the Iranian food composition table was used. Urinary net acid excretion is an indicator of NEAP, which is affected by dietary nutrient intake. Because it is difficult to directly measure NEAP, two indices recently have been introduced to characterize DAL from the diet. First, PRAL was estimated by applying the following formula, which was described by Remer et al. (8, 9, 16).

PRAL (mEq/d) = 0.4888 × protein intake (g/d) + 0.0366 × phosphorus (mg/d) – 0.0205 × potassium (mg/d) – 0.0125 × calcium (mg/d) – 0.0263 × magnesium (mg/d).

Moreover, NEAP was calculated based on the following algorithm, which was developed by Frassetto et al. (10):

NEAP (mEq/d) = [54.5 × protein intake (g/d) ÷ potassium intake (mEq/d)] – 10.2.

According to this concept (NEAP), the amount of sulfuric acid and bicarbonate production owing to protein and potassium (Pro/K) metabolism are considered to be the major determinants of DAL (10). The validity of the foregoing scores recently has been examined in comparison with 24-h urinary acid load in healthy adults (9, 10). Both PRAL and NEAP were established as reasonably valid measures for estimating DAL (9, 10).

2.3. Other measurements

We obtained demographic information by face to face interview. The bodyweight of participants was assessed to the nearest 100-gram, while they were wearing light clothes, with no shoes, and standing barefoot. Height was measured using a stadiometer and reported to the nearest 0.5 cm, with no shoes and shoulders in normal alignment. Body mass index (BMI) was computed as weight (in kilograms) divided by the square of height (in meters). Waist circumference (WC) was measured to the nearest 0.5 cm, using a tape meter, over light clothing, and without any pressure, at the level of the umbilicus. Participants' arterial blood pressure was measured manually, using a mercury sphygmomanometer with Korotkoff sound technique, after a 15-minute rest in sitting posture, twice within one minute from each other. The first onset of the tapping sound and disappearance of the sound were determined as systolic blood pressure (SBP) and diastolic blood pressure (DBP), respectively. The average of the two atrial blood pressure measurements was reported as the final atrial blood pressure for each participant. For biochemical assessment, 10 cc of venous blood was taken after 10-12 hours of overnight fasting and transferred to the research laboratory. Fasting blood glucose (FBG) was measured by the enzymatic colorimetric method, using glucose oxidase (Pars Azmoon, Tehran, Iran) and the Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands); with intra- and inter-assay coefficients of variation (CVs) being 1.1% and 1.4%, respectively. For assessment of serum TG levels, an enzymatic calorimetric method with glycerol phosphate oxidase was used (interassay CV: 0.6%; intraassay CV: 1.6%). Serum TC levels were determined with cholesterol esterase and cholesterol oxidase applying the enzymatic colorimetric method (interassay CV: 1.1%; intraassay CV: 1.4%). HDL-C was measured after precipitation of other lipoproteins using phosphotungstic acid and magnesium chloride fluid (interassay CV: 1.8%; intraassay CV: 1.5%). Serum LDL-C levels were measured after precipitation of LDL-C by using heparin and sodium citrate (interassay CV: 0.95%; intraassay CV: 1.4%). All the analyses were performed using commercial enzymatic reagents (Pars Azmoon, Tehran, Iran) and by applying an auto-analyzer system (Selectra E, Vitalab, Holliston, the Netherlands). Metabolic syndrome was defined as the presence of at least three criteria based on cook et al. study as follows: WC ≥ 90th percentile of national data for age and sex; SBP and DBP ≥ 90th percentile of NHLBI for age and sex; fasting TG level ≥110 mg/dL and HDL-C ≤ 40 mg/dL; and FBS level 100 mg/dL.

2.4. Statistical Analysis

We assessed the normality of distribution for variables using one-sample K-S. PRAL and NEAP were converted to the high and low category by the median value of them. Characteristics and nutritional state of participants across the median category of PRAL and NEAP were presented by mean ± SD and median (25-75 interquartile range) for normal and skewed distribution, respectively; and by percentages for categorical variables. T-test and Mann-Whitney tests were used to investigate the differences of continuous and categorical variables across the PRAL and NEAP categories, respectively. We defined two models as follows: model 1 was crude, model 2 adjusted for age, sex, BMI, and total energy. Odds ratios (OR) and 95% confidence intervals of MetS across PRAL and NEAP Category were assessed by logistic regression analysis. Furthermore, the association of PRAL and NEAP score with MetS components was evaluated by logistic regression analysis. All analyses were accomplished using IBM SPSS for Windows, version 20 (SPSS, Chicago, IL, USA); with the significance level set at P-value <0·05 (two-tailed).

3. Results

In this cross-sectional study, the general characteristic of participants (N = 500) for the total population was described in Table 1. The mean±SD age of participants was 12.9±2.5 years. Among participants, 53 % were girls. The median of PRAL and NEAP were -3.24 and -19.92, respectively. Dietary intake of participants for each category of PRAL and NEAP are presented in Table 2. Participants included in the highest category of PRAL were characterized by higher protein intakes (p<0.001), dietary cholesterol (p=0.026), whole grains (p<0.001), refined grains (p<0.001), and meats (p<0.001).

Table 1. Characteristic of participants according to the low and high category of PRAL and NEAP scores.

Variables	Median of PRAL (-3.24)		P-value	Median of NEAP (-19.92)		P-value
	Low N=251	High N=249		Low N=251	High N=249	
Age (year)	12.1±1.7	12.4±1.7	0.003	12.2±1.7	12.4±1.8	0.001
Girls (%)	56	31	0.003	53	42	0.001
BMI z-score	1.5±0.3	1.6±0.3	0.227	1.5±0.3	1.6±0.3	0.357

Data are presented as mean±standard deviation or N (%). Chi-square test was used for categorical variables; T-test or Mann-Whitney was used for continuous variables.

Table 2. Dietary intakes of participants according to the low and high category of PRAL and NEAP scores.

Variables	Median of PRAL (-3.24)		P-value	Median of NEAP (-19.92)		P-value
	Low N=251	High N=249		Low N=251	High N=249	
Acid load	-19.44±18.27	8.85±11.08		-18.10±0.20	-17.71±0.22	
Energy (kcal)	2865.7±881.4	274.0±888.5	0.922	2885.0±862.5	2854.7±907.0	0.889
Protein (percent)	12.6±2.0	14.0±2.2	<0.001	12.9±2.0	14.0±2.1	<0.001
Carbohydrate (percent)	56.6±5.7	55.8±5.6	<0.034	56.4±5.7	55.4±5.4	0.055
Fat (percent)	33.4±5.6	32.6±5.4	0.212	33.4±5.6	32.6±5.4	0.182
Dietary cholesterol (mg/day)	265.0±125.4	297.9±181.5	0.026	255.2±161.4	294.8±178.2	0.020
Total fiber (g/1000 kcal/day)	19.0±5.4	16.5±6.4	0.10	18.3±5.3	17.6±5.5	0.595
Sodium (g/1000 kcal/day)	1378.4±444.9	1457.1±447.0	0.083	1385.8±463.9	1453.7±374.0	0.113
Potassium (g/1000 kcal/day)	1659.0±313.0	1331.8±221.5	<0.001	1668.2±306.6	1322.5±216.3	<0.001
Calcium (g/1000 kcal/day)	503.8±133.7	486.0±131.6	0.273	517.2±138.6	472.6±132.2	0.003
Phosphorous (g/1000 kcal/day)	625.6±114.8	644.0±110.9	0.083	643.9±121.4	629.6±110.6	0.667
Magnesium (g/1000 kcal/day)	160.7±28.8	150.5±28.1	0.002	170.0±26.5	150.2±29.2	0.001
Whole grains (g/1000 kcal/day)	17.7±15.0	27.3±29.3	<0.001	17.5±14.1	27.6±29.7	0.001
Refined grains (g/1000 kcal/day)	109.9±39.3	141.0±63.9	<0.001	110.0±38.9	140.9±64.1	<0.001
Fruits (g/1000 kcal/day)	198.6±99.1	122.5±58.9	<0.001	198.0±99.3	123.1±59.4	<0.001
Vegetables (g/1000 kcal/day)	118.3±65.6	76.0±41.3	<0.001	118.0±65.5	76.4±41.8	<0.001
Dairy (g/1000 kcal/day)	191.6±100.3	193.1±106.7	0.892	205.9±107.7	178.8±97.3	0.016
Meats (g/1000 kcal/day)	25.4±12.8	36.4±18.7	<0.001	24.8±12.3	37.0±18.7	<0.001
Legumes (g/1000 kcal/day)	15.1±12.7	14.0±10.3	0.375	15.0±13.0	14.2±10.0	0.550
Nuts (g/1000 kcal/day)	6.4±8.2	3.9±4.2	<0.001	6.0±7.3	4.3±5.9	0.021

Data are presented as mean±standard deviation. T-test was used for continuous variables.

Furthermore, they showed lower intake of carbohydrates (p=0.034), potassium (p<0.001), Magnesium (p=0.002), fruits (p<0.001), vegetables (p<0.001), and nuts (p<0.001). Participants in the highest category of NEAP also were characterized by protein intakes (p<0.001), dietary cholesterol (p=0.020), whole grains (p=0.001), refined grains (p<0.001), and meats (p<0.001). However, they had lower intake of potassium (p<0.001), calcium (p=0.003), magnesium (p=0.001), fruits (p<0.001), vegetables (p<0.001), dairy (p=0.016), and nuts (p=0.021). Metabolic syndrome components of participants based on the low and high category of PRAL and NEAP scores were reported in Table 3. There were no significant differences between the category of PRAL and NEAP. Odds ratio (OR) and 95% confidence intervals (CI) for MetS and MetS components for each category of PRAL and NEAP are provided in Table 4. By using logistic

regression, no significant association was observed between PEAL and NEAP with metabolic syndrome (OR= 0.98, 95% CI: 0.55-1.55, p-value= 0.775 and OR= 0.88, 95% CI: 0.49-1.39, p-value= 0.418, respectively), after adjustment for potential confounders. There was no significant association between DAL and any of MetS components.

Table 3. MetS components based on low and high category of PRAL and NEAP scores.

Variables	Median of PRAL (-3.24)		P-value	Median of NEAP (-19.92)		P-value
	Low N=251	High N=249		Low N=251	High N=249	
WC (cm)	77.9±7.8	88.1±11.0	0.339	78.6±8.7	82.8±12.2	0.146
SBP (mmHg)	101.0 (91.0-114.0)	106.0 (97.0-118.5)	0.144	101.0(91.0-113.2)	106.0 (97.0-118.0)	0.217
DBP (mmHg)	61.0 (60.0-70.0)	69.0 (60.0-70.0)	0.176	61.0(60.0-70.0)	69.0 (60.0-70.0)	0.388
TG (mg/dl)	107.0 (76.2-144.7)	105.0 (74.5-138.5)	0.907	107.0 (76.2-143.5)	103.0 (74.0-141.0)	0.756
FBS (mg/dl)	90.7±8.6	90.5±9.8	0.797	90.9±8.7	90.3±9.7	0.706
HDL (mg/dl)	51.7±12.2	49.0±11.2	0.615	51.7±12.2	49.0±11.1	0.869
MetS (%)	49 (%29)	48 (%29)	0.923	50 (%30)	47 (%28)	0.700

WC, waist circumferences; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; FBS, fasting blood sugar; HDL, high density lipoprotein, MetS, metabolic syndrome.
Data are presented as mean±standard deviation or N (%) or median (interquartile range). Chi-square test was used for categorical variables; T-test or Mann-Whitney was used for continuous variables.

Table 4. Odds ratio (95% CI) for high WC, high BP, high TG, high FBS, low HDL, and MetS according to PRAL and NEAP category.

Variables		Median of PRAL (-3.24)		P-value	Median of NEAP (-19.92)		P-value
		Low N=251	High N=249		Low N=251	Low N=249	
High WC	Crude	1	1.52(0.65-3.44)	0.349	1	1.56(0.66-3.49)	0.342
	Adjusted model [a]	1	1.53(0.56-1.27)	0.501	1	1.34(0.59-3.45)	0.342
High BP	Crude	1	1.45(0.84-2.32)	0.193	1	1.45(0.79-2.17)	0.393
	Adjusted model [a]	1	1.21(0.70-2.08)	0.510	1	1.20(0.67-1.98)	0.718
High TG	Crude	1	0.97(0.58-1.38)	0.656	1	0.98(0.58-1.38)	0.726
	Adjusted model [a]	1	0.80(.49-1.27)	0.387	1	0.97(0.49-1.28)	0.345
High FBS	Crude	1	1.20(0.66-2.09)	0.595	1	1.1(0.55-1.76)	0.991
	Adjusted model [a]	1	1.11(0.58-2.05)	0.795	1	0.97(0.50-1.74)	0.929
Low HDL	Crude	1	1.30(0.73-2.11)	0.482	1	1.20(0.67-1.96)	0.666
	Adjusted model [a]	1	1.22(0.67-2.14)	0.566	1	1.31(0.62-1.97)	0.742
MetS	Crude	1	1.10(0.64-1.64)	0.923	1	0.97(0.57-1.46)	0.677
	Adjusted model [a]	1	0.98(0.55-1.55)	0.775	1	0.88(0.49-1.39)	0.418

WC, waist circumferences; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; FBS, fasting blood sugar; HDL, high density lipoprotein, MetS, metabolic syndrome.
[a] Model: adjusted for sex, age, BMI, and total energy.

4. Discussion

To the best of our knowledge, the present study is the first study on the association between DAL (both PRAL and NEAP scores) with MetS among children and adolescents. No significant association with any of MetS components was found. Although there was no study examining the association between DAL score and MetS in children and adolescents; only one study among Iranian women, observed that women with a higher DAL score had higher weight, waist circumferences, and serum triglyceride level in comparison with women who had a lower DAL score (18). This inconsistent finding might be justified by the difference in the age of studied populations (children vs. adults). Notably, the effect of age and environmental factors on the progression of MetS, are observed more accurately over time, which leads to the better observation of variations and increases in MetS and MetS components among adults rather than children. Besides, different results could be achieved if we follow-up on our sample. Results from Aslani et al. (19) study indicated that students with higher NEAP had greater neck circumferences. Furthermore, there was an inverse association between PRAL and NEAP with parental BMI. However, there was no significant association between PRAL and NEAP with other anthropometric indices. In our study, we did not observe a significant association between DAL and anthropometric indices. The large sample size (5326 vs. 500) is the most important difference between the aforementioned study and ours. Similar to our study, Rotterdam (20) and Kucharska (21) studies did not observe a significant association between DAL and blood pressure. Likewise, in our study and Iranian women study the higher PRAL category consumes a higher intake of protein and dietary cholesterol. Higher intake of meat was observed in both high PRAL and high NEAP category. In the present study, the PRAL ranged from -111.70 to 95.01, with a mean of -4.23 mEq/day. The NEAP ranged from-19.76 to -15.45, with a mean of -19.70 mEq/day. While, in Iranian women's study, the mean of PRAL and NEAP were 9.61 and 47.46 mEq/day, respectively (18). Higher mean of DAL score in Iranian women study in comparison with the present study

would be a substantial difference which might affect the relationship of DAL with MetS. Furthermore, compared with Iranian women's study, total fermentable fiber consumption among our participants was higher and it can regulate the activity of gut microbiota, which could be a cause of the nonsignificant association. For this study, we also acknowledge some limitations. First, the cross-sectional design is the most important. Therefore, we could not interpret the present results as a cause and effect relationship. Second, if we surveyed a larger sample size, we could perform sex-stratified analysis and observe the associations regarding gender. Third, despite controlling many potential confounders, several other confounders may still affect the association between DAL score and MetS. Despite limitations, the present study has strength as well. This is the first study conducted to evaluate the association between DAL and MetS among children and adolescents.

5. Conclusion

In conclusion, our findings could not show a significant association between DAL and MetS. As the progression of Mets and CVD begins from childhood, it is important to evaluate the relation between DAL and Mets among children and adolescents. Research within a cohort design is required to elucidate the association between diet acid load and MetS among children and adolescents.

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