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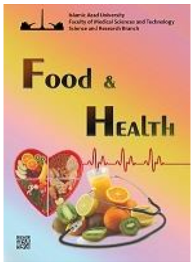

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The association of dietary acid load with non-alcoholic fatty liver disease among Iranian adults

Pegah Rahbarinejad[1*], Maryam Mohamadi Narab[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 the dietary acid load (DAL), has been related to risk factors for non-alcoholic fatty liver (NAFLD). In the current study, we investigated the association between DAL and NAFLD among Iranian adults. This cross-sectional study was conducted on 675 participants, aged 20-60 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 NAFLD according to the PRAL and NEAP categories. The mean age of the participants was 38.1 ± 8.8 years old. The median of PRAL and NEAP were -8.13 and -9.05 mEq/day, respectively. In this study, the potential confounders including age, sex, leisure time activity, and total energy were adjusted in the multivariable-adjusted model. By using logistic regression, no significant association was observed between PEAL and NEAP with NAFLD. (OR=1.03, 95% CI: 0.66-1.60, P-value=0.905 and OR=1.12, 95% CI: 0.72-1.75, P-value=0.611, respectively) after adjustment for potential confounders. Longitudinal studies should be conducted to evaluate the association between PRAL and NEAP with NAFLD among adults.

1. Introduction

Nonalcoholic fatty liver (NAFLD) is characterized by abnormal chemistry worldwide (1). NAFLD may progress to nonalcoholic steatohepatitis (NASH), cirrhosis, liver failure, and liver cancer and is demonstrated to be an independent cardiovascular risk factor (2). The underlying causes of NAFLD include obesity, hyperinsulinemia, hypertension, type 2 diabetes, and hypertriglyceridemia (3). Besides of all modifiable and non-modifiable health determinants, diet is one of the most important determinants which can ameliorate or deteriorate chronic conditions, as well as NAFLD (4, 5). Adherence to healthy dietary patterns can play a key role in preventing some chronic diseases including NAFLD (4, 5). 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 (6-8). 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 (9). The PRAL score is based on dietary intakes of protein, potassium, calcium, magnesium, and phosphorous (9, 10). NEAP is calculated using total protein and potassium, which are the crucial determinants of metabolic acidosis (11). Both scores have been validated against objective measures of acid-base load determined from 24-h urine in healthy adults (10, 11). 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 (10-13). Higher consumption of animal products and processed should be compensated by higher consumption of fruits and vegetables due to reducing metabolic acidosis (14). As animal products contain a higher value of protein and potassium, they lead to produce more potential inorganic and endogenous acid (14). However, alkaline foods such as fruit and vegetable encompass higher magnesium and potassium content which can neutralize acid-derived food intake (15, 16).

*Corresponding author: Department of Nutrition, Science and Research Branch, Islamic Azad University, Tehran, Iran.
E-mail address: pegah.rahbarinejad@gmail.com (Pegah Rahbarinejad).

The literature suggests that the achievements of ideal acid-alkaline balance can prevent metabolic acidosis. Since metabolic acidosis and NAFLD are both related to reduced levels of GH and IGF-I, it is possible to consider that diet-induced acid load may constitute a nutritional factor with an influence on NAFLD development (17). To our knowledge, there is limited literature on the association between DAL with NAFLD. As the progression of NAFLD is related to CVD, it is important to evaluate the relation between DAL and NAFLD among adults. To date, no study has examined the association between DAL and NAFLD among Iranian adults. Therefore, the aim of the current study was to evaluate the association of DAL with NAFLD among Iranian adults.

2. Material and methods

2.1. Participants

This cross-sectional study was conducted on 675 Iranian adults, aged 20-60 years. Individuals were eligible for inclusion if they had no known medical illnesses such as diabetes, kidney, or cardiovascular disease (based on physician examination and medical records review).

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 participants 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. (9, 10, 18).

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. (11):

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 (11). The validity of the foregoing scores recently has been examined in comparison with 24-h urinary acid load in healthy adults (10, 11). Both PRAL and NEAP were established as reasonably valid measures for estimating DAL (10, 11).

2.3. Other measurements

We obtained demographic information by face to face interview. Bodyweight of participants was assessed using the scale of GAIA 359 PLUS, 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 square of height (in meters). Physical activity was evaluated using the metabolic equivalent task (MET) questionnaire. NAFLD was diagnosed by a gastroenterologist based on the results of ultrasound and fibroscan examination.

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 in 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, physical activity, and total energy. Odds ratios (OR) and 95% confidence intervals of NAFLD across PRAL and NEAP Category were assessed 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 = 675) for the total population was described in Table 1. The mean±SD age of participants was 38.1 ± 8.8 years. Among participants, 53% were men. The median of PRAL and NEAP were -8.13 and -9.05 mEq/day, respectively. The dietary intake of participants for each category of PRAL and NEAP are presented in Table 2. Participants included in the higher category of NEAP were characterized by higher protein intakes (P<0.001). Compared to the higher category of PRAL, the lower one had a significantly higher intake of energy (P<0.006). Odds ratio (OR) and 95% confidence intervals (CI) for NAFLD for each category of PRAL and NEAP are provided in Table 3. By using logistic regression, no significant association was observed between PEAL and NEAP with NAFLD (OR= 1.03, 95% CI: 0.66-1.60, P-value= 0.905 and OR= 1.12, 95% CI: 0.72-1.75, P-value= 0.611, respectively), after adjustment for potential confounders.

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

Variables	Median of PRAL (-8.12)		P-value	Median of NEAP (-9.05)		P-value
	Low N=337	High N=338		Low N=337	High N=338	
Age (year)	38.6±9.1	37.6±8.6	0.156	38.7±9.0	37.5±8.7	0.087
Men (%)	49	57	0.034	48	58	0.005
Smoking (%)	5	3	0.244	4	4	0.706
BMI (kg/m^2)	26.7±4.1	27.0±4.5	0.361	26.7±4.1	27.0±4.5	0.313

Data are presented as mean±standard deviation or N (%). Chi-square test was used for categorical variables; T-test 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 (-8.12)		P-value	Median of NEAP (-9.05)		P-value
	Low N=337	High N=338		Low N=337	High N=338	
Acid load	-23.62±14.66	4.10±9.71		-9.22±0.12	-8.79±0.22	
Energy (kcal)	2285.3±577.9	2152.6±658.3	0.006	2223.4±575.7	2214.3±667.0	0.848
Protein (percent)	13.4±2.1	14.0±2.2	0.229	12.8±2.0	14.0±2.5	<0.001
Carbohydrate (percent)	55.5±8.5	56.4±6.9	0.502	56.6±5.7	56.4±7.0	0.055
Fat (percent)	33.1±9.2	31.2±6.6	0.150	33.4±5.6	31.4±6.9	0.182
Dietary cholesterol (mg/day)	222.9±107.5	226.6±155.7	0.718	217.7±105.8	231.9±156.7	0.167

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

Table 3. Odds ratio (95% CI) for NAFLD according to PRAL and NEAP category.

Variables		Median of PRAL (-8.12)		P-value	Median of NEAP (-9.05)		P-value
		Low N=337	High N=338		Low N=337	Low N=338	
NAFLD	Crude	1	1.18(0.86-1.63)	0.301	1	1.29(0.94-1.78)	0.115
	Adjusted model a	1	1.03(0.66-1.60)	0.905	1	1.12(0.72-1.75)	0.611

NAFLD, non-alcoholic fatty disease. [a] Model: adjusted for sex, age, BMI, physical activity, 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 NAFLD among Iranian adults. No significant association was found between the DAL score and NAFLD. Although there was no study examining the association between DAL score and NAFLD among Iranian adults; only one study among young adulthood, observed a significant association of the diet-dependent acid load (PRAL) during adolescence with surrogates of NAFLD in young adult females but not males (19). A study of Hong Kong Chinese adults showed that higher estimated NEAP but not PRAL was associated with an increased likelihood of having NAFLD, while both markers of DAL were not associated with the presence of possible advanced fibrosis (17). This inconsistent finding might be justified by the difference in outcome measures, the age range, sample size, as well as the dietary intakes. There is a complex relationship between protein intake and NAFLD risk. A higher intake of protein induces a higher value of NEAP and PRAL (17). It is in line with our finding that higher intake of protein-induced higher NEAP value. The acid base balance can disturb by higher intake of protein which contributes to GH resistance in the liver and higher risk of NAFLD. Therefore, the magnitude of the effect of diet on NAFLD remains to be examined (17). The justification for no significant association in the present study is that adults with higher DAL score may suffer from health consequences. This condition could lead to cardio-metabolic interventions or treatments (such as medication use or exercise), reducing the risk of having criteria for NAFLD among those in higher PRAL and NEAP values. 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 NAFLD. Despite the limitations, the present study has strengths as well. This is the first study conducted to evaluate the association between DAL and NAFLD among Iranian adults. Moreover, due to the wide variety of socio-economic status in these populations, a little difference in dietary intake can make a difference in disease risk.

5. Conclusion

In conclusion, our findings could not show a significant association between DAL and NAFLD. As the progression of NAFLD is related to many chronic conditions, it is important to evaluate the relation between DAL and NAFLD among adults. Research within a cohort design is required to elucidate the association between diet acid load and NAFLD among Iranian adults.

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