European Review for Medical and Pharmacological Sciences 2023; 27: 2443-2452

Examining dietary acid load in individuals with type 2 diabetes: a case-control study

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Abstract. – OBJECTIVE: Diabetes is a chronic disease that can cause various complications and has a high prevalence. Evidence increasingly shows that acid-base homeostasis is critical to maintaining normal metabolic function. This case-control study aims to evaluate the relationship between dietary acid load and the risk of type 2 diabetes.

PATIENTS AND METHODS: This study recruited 204 participants, 92 of whom had just been diagnosed with type 2 diabetes, and 102 healthy controls who were matched in age and gender as controls. Twenty-four dietary recall was used for dietary intake assessments. Dietary acid load was approximated using two different methods: potential renal acid load (PRAL) and net endogenous acid production (NEAP), both calculated from dietary recalls.

RESULTS: In the case and control groups, the dietary acid load mean scores were 4.18±26.8, 20.84±29.54 mEq/day for PRAL, and 55.11±29.23, 68.43±32.23 mEq/day for NEAP, respectively. When it came to the multiple possible confounders, the participants in the highest tertile of PRAL (OR 4.43, 95% CI: 1.38-23.81, p_{trend}<0.001) and NEAP (OR: 3.15, 95% CI: 1.53-9.59, p_{trend}<0.001) had a significantly higher risk of developing type 2 diabetes compared to those in the lowest tertile.

CONCLUSIONS: The findings of the present study suggest that a high acid load in the diet may increase the risk of type 2 diabetes. Therefore, it is possible that limiting dietary acid load could lower type 2 diabetes risk in vulnerable individuals.

Key Words:
Dietary acid load, Type 2 diabetes, Potential renal acid load, Net endogenous acid production.

Introduction

Type 2 diabetes is a multifaceted disease that affects both genes and environmental factors and is increasing worldwide[1,2]. More than 90% of diabetic patients suffer from type 2 diabetes. It can cause microvascular and macrovascular difficulties for patients, as well as psychological and physical problems for both patients and caregivers. Consequently, it poses a significant financial burden on the healthcare system[3]. Therefore, determining the environmental risk factors that contribute to diabetes allows for a more accurate assessment of the onset or course, and the development of innovative treatments for diabetes is a significant challenge for the healthcare system[4,5].

Many medical professionals[6,7] think that the best way to manage diabetes is through a combination of diet modification and conventional medical treatment. Leading a healthy diet is critical to reduce a person's risk of developing type 2 diabetes. Today, the Western diet is centered around foods rich in animal proteins and low in fruit and vegetables, alongside processed and refined food[8]. This diet produces endogenous acid because it includes grains, rice, meat, fish, and cheese and contains foods low in alkaline such as legumes, fruits, vegetables, potatoes and red wine[9-11].

The composition of the diet consumed by individuals affects the acid-base balance of the body, which is of vital importance in maintaining metabolic health[12]. The dietary components that release acid precursors after metabolism are phosphorus and proteins (mainly the sulphur-containing amino acids, such as cysteine, methionine, and taurine, as well as cationic amino acids such as lysine and arginine). The nutrients that are precursors to alkali are potassium, magnesium, and calcium[13]. After food has been ingested, the stomach wall excretes hydrogen ions, and the pancreas secretes alkali into the digestive tract. By absorbing sulphur amino acids and alkali salts, which are transported to the liver and metabolically active tissues as substrates, the gastrointestinal tract influences the acid-base balance. Once oxidized, sulphur amino acids release protons and organic acids release alkali, which have an effect on the acid-base reserve and are ultimately excreted by the kidneys. Although the intestine does not produce acids or bases, the characteristics of the diet determine the formation

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of acids and alkalis after absorption and metabolism in the liver[13,14]. Lungs, kidneys, and various chemical buffering systems of a healthy person maintain acid-base homeostasis[12].

Most studies[15,16] on the dietary acid load have frequently used the potential acid load (PRAL)[15] and net endogenous acid production (NEAP)[16]. The higher the PRAL and NEAP score is, the more acid the diet in question generates[17]. The consumption of acidogenic diets cause low-grade metabolic acidosis. This metabolic acidosis could change insulin binding affinity with its receptors. Disrupting insulin binding to receptors inhibits the initial step of the insulin signalling pathway, which may result increase in hepatic gluconeogenesis and a decrease in muscle uptake of glucose, leading to insulin resistance and type 2 diabetes[17,18]. Diets with high acid load induce a low-grade metabolic acidosis state, which is also associated with the development of metabolic alterations such as abdominal obesity[19,20], kidney disease[21,22], high blood pressure[23,24], abnormal lipid profiles[25], bone health[26], migraine[27], sleep quality and mental health[28]. However, recommendations for the dietary acid load of those with type 2 diabetes are currently insufficient; hence further studies are required.

Dietary habits also differ significantly from one society to the next. According to the literature review, there were no studies that evaluated link between dietary acid load and risk of type 2 diabetes in Turkish adults. This case-control study aims to evaluate the association between dietary acid load and risk of type 2 diabetes in Turkish people.

Patients and Methods

Participants

This was an age-gender matched case-control study conducted on 92 people who had recently been diagnosed with type 2 diabetes according to American Diabetes Association (ADA) criteria[29] and applied to outpatient internal medicine clinic of Gaziantep University Şahinbey Research and Application Hospital, and 102 healthy adults. The American Diabetes Association (ADA) defines newly diagnosed diabetes as diagnostic criteria: a fasting plasma glucose (FPG) level of ≥126 mg/dL or 2 h postprandial plasma glucose level of ≥200 mg/dL during the oral glucose tolerance test (OGTT) or random plasma glucose ≥200 mg/dL with classic symptoms of hyperglycaemia or HbA1c≥6.5 mg/dL. Diabetics were excluded if they had any history of other chronic disease (e.g., cardiovascular disease, kidney disease, liver and lung disease), following a specific diet or physical activity, were pregnant and were lactating and daily energy intake was outside the range of 800-4,200 kcal. The control group were randomly selected from those who were residing in Gaziantep province and had blood glucose check-ups within the last six months. The exclusion criteria for the controls were determined as follows: suffering from chronic diseases that may affect their usual eating behaviors, adhering to a particular lifestyle (diet and/or physical activity) using medications that affect their weight and diet, being pregnant and lactating, and having a family history of diabetes or hypertension and daily energy intake was outside the range of 800-4,200 kcal.

The present study was carried out based on Declaration of Helsinki principles, and study protocol was approved by Gaziantep Islam Science Technology University (protocol no: 2022/120 approval date: 07.06.2022). All participants signed the informed consent form.

Data Collection

Participants were interviewed face to face to collect demographic information (age, gender, marital status, smoking and educational background), anthropometric measures were performed, and twenty-four hour dietary recall were obtained.

Evaluation of Anthropometric Measurements

Body weight was measured by using a body composition monitor scale TANITA BC-730 (TANITA Corp., Tokyo, Japan) while wearing light clothes and without shoes. Their height was measured to the nearest 0.1 cm using SECA 213 stadiometer (SECA Corp., Hamburg, Germany). Waist circumference (WC) was measured from the center point between the lower rib bone and the crystal iliac bone, and hip circumference was measured from the widest point of the hip while standing on the side with an inflexible measuring tape. The body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. To calculate the waist hip ratio (WHR), WC was divided by the circumference of the hip and the waist height ratio (WHtR) was calculated by dividing the WC by height. All measurements were obtained as described previously[30] and taken by a trained dietician.

Calculation of Dietary Acid Load

Dietary intake was evaluated using 24-hour diet recall as it was less biased than food frequency questionnaires[31]. For recalls, the same trained dietitian conducted face-to-face interviews. The photographic atlas[32] was utilized to identify the portion sizes of the foods consumed. The energy, macronutrient and micronutrient intake of the participants was calculated using BeBIS 7 software (Ebispro, Stuttgart, Germany).

The dietary acid load was estimated from dietary composition data using two proven methods: Potential renal acid load (PRAL)[15], and net endogenous acid production (NEAP)[16]. The following algorithms are used for these two measurements:

PRAL (mEq/day) = [0.4888 x protein (g/day)] + [0.0366 x phosphorus (mg/day)] - [0.0205 x potassium (mg/day)] - [0.0263x magnesium (mg/day)] - [0.0125x calcium(mg/day)]; NEAP (mEq/day) = [(54.59 x protein (g/day) / potassium (mEq/day)] -10.2.

Statistical Analysis

The normal distribution of the continuous variables was analysed using the Kolmogorov-Smirnov test. Descriptive statistics were expressed as mean with standard deviation for continuous variables. Categorical variables were presented as numbers and percentages. The independent sample *t* test and the Chi-square test were used to compare demographic characteristics, anthropometric measurements and dietary intake between the case and control groups. The chi-square test and one-way analysis of variance (ANOVA) were used to compare categorical and continuous variables, respectively, based on the PRAL and NEAP tertiles. Multivariate logistic regression models were used to explore the association between dietary acid load and the risk of type 2 diabetes after adjusting for age, gender, BMI, and smoking status as well as daily energy, carbohydrate (g), total fat (g) and sodium (mg) intake. The median value of dietary acid load for each tertile was used as a continuous variable, so that linear trends could be seen in the tertiles. All analyses were performed with SPSS v. 23 (IBM Corp., Armonk, NY, USA). The significance level was accepted as $p<0.05$.

Results

Table I shows the comparison of demographic information, anthropometric measurements and dietary intake. The prevalence of Type 2 diabetes was 45.1% among participants. Both the case group and the control group were composed of 55.4% males. The mean age of the participants in the case group was 47.70±8.45; those in the control group had a mean age of 47.20±7.25 ($p>0.05$). The case group's mean scores of the dietary acid load were significantly higher than those of the control group: PRAL (20.84 ± 29.54 *vs.* 4.18±26.8 mEq/day, respectively, $p<0.001$) and NEAP (68.43±32.23 *vs.* 55.1 ±29.23 mEq/day, respectively, $p<0.05$). Also, the case group had higher body weight, BMI, WC, WHR, and WHtR ($p<0.001$) as well. Furthermore, the intake of energy, carbohydrate, protein, phosphorus and calcium was higher in the cases ($p<0.05$). However, both groups' total fat, saturated fatty acids (SFA), monounsaturated fatty acid (MUFA), polyunsaturated fatty acid (PUFA), fiber, sodium, potassium and magnesium intake did not differ significantly one another (Table I).

People in the third tertile of PRAL and NEAP scores were more likely to be male than those in the lowest tertile ($p<0.05$). The rates of current smokers in the third PRAL and NEAP tertiles, respectively, is 51.4% and 49.3%. The mean WHR and NEAP score were higher among participants in the third tertile PRAL than those in the first tertile ($p<0.05$). Similarly, participants in the third tertile of the NEAP had significantly higher mean WHR and PRAL score than participants in the first tertile ($p<0.05$). Participants whose PRAL and NEAP scores were in the third tertile tended to have a higher intake of energy, carbohydrates, total fat, calcium, and phosphorus ($p<0.05$) (Table II a-b).

Table III displays the odds ratios (ORs) and confidence intervals (Cls) for type 2 diabetes according to the tertiles of dietary acid load. In the first model, OR with Cl of type 2 diabetes for the lowest (first), medium (second) and highest (third) tertiles of PRAL scores – after adjustment for age and gender – were 1.00 (reference), 1.85 (0.67-3.15) and 2.69 (1.40-10.99), respectively ($p_{trend}<0.001$). In the second model, after adjusting for age, gender, BMI, and smoking status, the risk of type 2 diabetes in the third tertile relative to first tertile of PRAL score was 2.04 (1.36-11.61). In the third model, additional adjustments for energy, carbohydrate, total fat, and sodium intake increased the link between PRAL score and risk of type 2 diabetes in the participants who were in the third tertile compared to those in the lowest tertile (OR: 4.43; 95% Cl: 1.38-23.81). For NEAP scores, in the first model after adjusted for age and gender, the OR (95% Cls) of type 2 diabetes for lowest through the highest NEAP tertiles were 1.00 (reference), 1.63 (1.03-5.06) and 2.33 (1.94-6.72), re-

Table I. Comparison of demographic characteristics, anthropometric measurements, and dietary intake among the case-control group.

	Case (n: 92) n (%)	Control (n: 112) n (%)	p
Gender			
Male	51 (55.4)	62 (55.4)	0.989*
Female	41 (44.6)	50 (44.6)	
Marital status			
Single	18 (19.6)	26 (23.2)	0.609*
Married	74 (80.4)	86 (76.8)	
Smoking			
Yes	34 (37.0)	42 (37.5)	<0.001*
No	40 (43.5)	68 (60.7)	
Quit	18 (19.6)	2 (1.8)	
	$\bar{X}$ ± SD	$\bar{X}$ ± SD	
Age (years)	47.70 ± 8.45	47.20± 7.25	0.650**
Educational background (years)	11.1 ± 4.76	12.5 ± 4.59	0.030**
Body weight (kg)	84.12± 14.66	77.44± 1.55	<0.001**
BMI (kg/m^2)	29.08 ± 4.42	27.05 ± 4.38	0.001**
WC (cm)	103.79 ± 12.61	93.27 ± 11.40	<0.001**
WHR	0.95±0.09	0.87±0.06	<0.001**
WHtR	0.62±0.08	0.55±0.07	<0.001**
PRAL (mEq/day)	20.84 ± 29.54	4.18 ± 26.80	<0.001**
NEAP (mEq/day)	68.43 ± 32.23	55.11 ± 29.23	0.002**
Dietary intake			
Energy (kcal)	2345.84 ± 554.84	2113.56 ± 643.69	0.010**
Protein (g)	102.5 ± 42.23	84.03 ± 29.76	<0.001**
Protein (%)	17.66 ± 3.89	16.24 ± 3.25	0.007**
Carbohydrate (g)	201.93 ± 51.40	225.08 ± 77.03	0.015**
Carbohydrate (%)	39.42 ± 8.56	43.13 ± 7.08	0.001**
Total fat (g)	104.24 ± 41.73	97.2 ± 34.93	0.191**
Total fat (%)	42.05 ± 7.54	40.51 ± 6.40	0.115**
SFA (g)	32.35 ± 11.86	30.88 ± 10.04	0.341**
MUFA(g)	38.83 ± 22.18	35.82 ± 17.55	0.279**
PUFA(g)	26.2 ± 11.39	24.09 ± 9.69	0.154**
Fibre (g)	25.03 ± 8.10	26.69 ± 9.34	0.181**
Sodium (mg)	2127.83 ± 824.98	2253.79 ± 1118.85	0.370**
Potassium (mg)	2948.25 ± 976.64	2963.47 ± 864.51	0.906**
Calcium (mg)	891.31 ± 321.56	777.1 ± 267.09	0.006**
Magnesium (mg)	322.23 ± 99.81	314.96 ± 114.43	0.623**
Phosphorus (mg)	1418.78 ± 455.55	1176.51 ± 321.01	<0.001**

BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, WHtR: Waist height ratio, SFA: Saturated fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids, *Chi-square test, **Independent samples *t*-test.

spectively (p_{trend}<0.001). In the second model after adjusting for age, gender, BMI, and smoking status, the OR (95% Cl) of type 2 diabetes in the highest tertile relative to lowest tertile of NEAP score was 2.68 (95% Cl: 1.40-8.87). In the third model, after adjusting potential confounding variables (energy, carbohydrate, total fat, and sodium intake), it was found that there was a stronger link between the NEAP score and the risk of type 2 diabetes in the participants who were in the third tertile compared to those in the lowest tertile (OR: 3.15, 95% Cl: 1.53-9.59) (Table III).

Table IIa. Demographic characteristics, anthropometric measurements and dietary intake of participants by dietary acid load tertile.

	PRAL			
	T1	T2	T3	*p*
PRAL (Median)	(-)16.88	13.60	40.59	
PRAL (Min-Max)	(-)58.14 – (-)3.94	(-) 2.22 – 22.15	22.80 – 79.27	
Gender n (%)				
Male	27 (40.3)	39(58.2)	47 (67.1)	0.006*
Female	40 (59.7)	28 (41.8)	23(32.9)	
Marital status n (%)				
Single	17 (25.4)	8(11.9)	19 (27.1)	0.063*
Married	50 (74.6)	59(88.1)	51 (72.9)	
Smoking n (%)				
Yes	21 (31.3)	19 (28.4)	36 (51.4)	0.007*
No	43 (64.2)	38 (56.7)	27 (38.6)	
Quit	3 (4.5)	10 (14.9.6)	7 (10.0)	
Age (years)	48.21 ± 7.61	48.15 ± 8.01	45.97 ± 7.67	0.158**
Educational background (years)	11.63 ± 4.68	12.09 ± 4.06	11.84 ± 5.33	0.852**
Body weight	78.02 ± 14.06	81.14 ± 12.37	82.13 ± 13.65	0.176**
BMI (kg/m^2)	28.1 ± 4.32	27.5 ± 4.39	28.3 ± 4.80	0.565**
WC (cm)	95.52 ± 13.74	98.34 ± 11.92	100.1 ± 13.14	0.117**
WHR	0.88 ± 0.10	0.91 ± 0.09	0.93 ± 0.09†	0.011**
WHtR	0.58 ± 0.08	0.58 ± 0.07	0.59 ± 0.08	0.450**
NEAP (mEq/day)	30.63 ± 10.57	58.60 ± 13.40†	92.76 ± 26.74†	<0.001**
Dietary Intake				
Energy (kcal)	1905.25 ± 539.04	2059.65 ± 416.34	2669.84 ± 659.12†	<0.001**
Protein (g)	68.77 ± 23.52	84.41 ± 21.62†	122.53 ± 39.02†	<0.001**
Protein (%)	15.85 ± 3.51	17.06 ± 2.98	17.70 ± 4.05†	0.009**
Carbohydrate (g)	199.58 ± 73.28	201.69 ± 55.07	241.44 ± 65.36†	0.007**
Carbohydrate (%)	44.48 ± 7.70	40.87 ± 7.28†	39.14 ± 8.07†	<0.001**
Total Fat (g)	80.16 ± 25.71	96.11 ± 26.06†	123.8 ± 45.20†	<0.001**
Total fat (%)	39.73 ± 7.36	42.01 ± 6.18	41.84 ± 7.15	0.105**
SFA (g)	26.54 ± 8.38	29.52 ± 7.70	38.26 ± 12.30†	<0.001**
MUFA (g)	28.19 ± 11.07	34.78 ± 14.02†	48.07 ± 25.32†	<0.001**
PUFA (g)	19.85 ± 9.16	25.57 ± 7.66†	29.51 ± 11.94†	<0.001**
Fibre (g)	24.22 ± 9.01	24.99 ± 7.07	28.50 ± 9.64†	0.009**
Sodium (mg)	1946.90 ± 950.01	2110.13 ± 933.09	2518.84 ± 1026.60†	0.002**
Potassium (mg)	3587.66 ± 736.12	2675.60 ± 700.42†	2621.55 ± 946.35†	<0.001**
Calcium (mg)	733.94 ± 286.04	803.68 ± 223.78	943.07 ± 334.55†	<0.001**
Magnesium (mg)	298.36 ± 125.70	324.85 ± 97.10	330.95 ± 97.57	0.174**
Phosphorus (mg)	1019.75 ± 230.83	1239.42 ± 239.05†	1584.74 ± 464.03†	<0.001**

BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, WHtR: Waist height ratio, SFA: Saturated fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids, *Chi-square test, **ANOVA, †Significantly different. from the lower tertile values at $p<0.05$ by post-hoc analyses.

Discussion

In this study, the acid load of the diet was determined using PRAL and NEAP. Both techniques evaluate the consumption of acid-base precursors, including calcium, magnesium, phosphorus, potassium, and protein, all of which preserve the acid-base balance[9,15]. The results of the present study revealed that the dietary acid load was directly correlated with the risk of developing type 2 diabetes. People with PRAL scores in the third tertile are approximately four times more likely to have type 2 diabetes than people with scores in the lowest tertile. In addition to this, those who scored

Table IIb. Demographic characteristics, anthropometric measurements and dietary intake of participants by dietary acid load tertile.

	NEAP			
	T1	T2	T3	*p*
NEAP (Median)	29.56	56.79	87.59	
NEAP (Min-Max)	31.68 – 9.03	43.13 – 69.60	69.62 – 157.01	
Gender n (%)				
Male	24 (35.8)	44 (64.7)	45 (65.2)	<0.001*
Female	43 (64.2)	24 (35.3)	24 (34.8)	
Marital status				
Single	17 (25.4)	11 (16.2)	16(23.2)	0.397*
Married	50 (74.6)	57 (83.8)	53(76.8)	
Smoking n (%)				
Yes	18 (26.9)	29 (42.6)	29 (42.0)	0.002*
No	47 (70.1)	27 (39.7)	34 (49.3)	
Quit	2 (3.0)	12 (17.6)	7 (8.7)	
Age (years)	49.07 ± 7.13	47.94 ± 7.71	45.3 ± 8.13†	0.014**
Educational background (years)	11.36 ± 4.74	12.57 ± 4.02	11.62 ± 5.26	0.288**
Body weight	77.66 ± 13.71	82.55 ± 13.27	81.1 ± 13.04	0.094**
BMI (kg/m^2)	28.58 ± 4.64	27.69 ± 4.44	27.66 ± 4.43	0.403**
WC (cm)	96.09 ± 13.09	99.63 ± 14.06	98.3 ± 11.81	0.282**
WHR	0.88 ± 0.09	0.91 ± 0.10	0.92 ± 0.08†	0.026**
WHtR	0.59 ± 0.08	0.59 ± 0.09	0.58 ± 0.07	0.897**
PRAL (mEq/day)	(-)18.88 ± 16.70	13.45 ± 15.64†	39.65 ± 17.83†	<0.001**
Dietary Intake				
Energy (kcal)	1874.38 ± 499.98	2150.88 ± 483.69†	2618.75 ± 682.19†	<0.001**
Protein (g)	64.27 ± 19.10	91.88 ± 23.79†	120.09 ± 40.19†	<0.001**
Protein (%)	15.28 ± 3.07	17.71 ± 3.11†	17.62 ± 4.07†	<0.001**
Carbohydrate (g)	194.86 ± 62.83	205.77 ± 63.34	242.58 ± 67.66†	<0.001**
Carbohydrate (%)	44.67 ± 7.07	39.69 ± 7.69†	40.09 ± 8.25†	<0.001**
Total FAT (g)	79.24 ± 25.52	102.11 ± 29.15†	119.18 ± 45.70†	<0.001**
Total Fat (%)	40.07 ± 7.08	42.49 ± 6.32	41.04 ± 7.34	0.129**
SFA (g)	26.14 ± 8.32	31.79 ± 8.45†	36.56 ± 12.74†	<0.001**
Mufa (g)	27.68 ± 11.76	37.22 ± 15.29†	46.35 ± 25.08†	<0.001**
PUFA(g)	19.98 ± 8.55	26.45 ± 9.16†	28.58 ± 11.70†	0.062**
Fibre (g)	28.69 ± 8.61	27.19 ± 7.44†	22.14 ± 9.06†	<0.001**
Sodium (mg)	1848.91 ± 910.97	2127.39 ± 858.56	2603.56 ± 1068.79†	<0.001**
Potassium (mg)	3478.03 ± 764.57	2948.76 ± 756.26†	2458.03 ± 919.52†	<0.001**
Calcium (mg)	696.26 ± 257.27	863.25 ± 249.54†	922.98 ± 333.80†	<0.001**
Magnesium (mg)	294.92 ± 121.13	332.77 ± 93.75	326.56 ± 105.01	0.091**
Phosphorus (mg)	1064.53 ± 255.22	1357.33 ± 339.53†	1430.07 ± 488.10†	<0.001**

BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, WHtR: Waist height ratio, SFA: Saturated fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids, *Chi-square test, **ANOVA, †Significantly different from the lower tertile values at $p<0.05$ by post hoc analyses.

in the third tertile of NEAP had about three times risk of type 2 diabetes than those whose scores were in the first tertile. Furthermore, those who scored in the third tertile of NEAP were at three times greater risk of developing type 2 diabetes than those whose scores were in the first tertile. The higher one's PRAL and NEAP score was, the more acidic foods they consumed; the lower the score, the more alkaline their diets were[27]. Diet is crucial for treating type 2 diabetes; consequently, it is important to study the unclear aspects of diet when treating type 2 diabetes[33].

Table III. Odds ratio and 95% confidence interval for type 2 diabetes according to tertiles.

	T1	T2	T3	p_{trend}
PRAL				
Model 1	1.00	1.85 (0.67-3.15)	2.69 (1.40-10.99)	<0.001
Model 2	1.00	1.42 (1.08-4.47)	2.04 (1.36-11.61)	<0.001
Model 3	1.00	2.26 (1.34-6.60)	4.43 (1.38-23.81)	<0.001
NEAP				
Model 1	1.00	1.63 (1.03-5.06)	2.33 (1.94-6.72)	<0.001
Model 2	1.00	1.81 (1.12-7.04)	2.68 (1.40-8.87)	<0.001
Model 3	1.00	1.98 (1.32-7.73)	3.15 (1.53-9.59)	<0.001

Model 1; adjusted for age and gender. Model 2; additionally, adjusted for BMI and smoking. Model 3; additionally, adjusted for energy, carbohydrate, total fat, and sodium intake.

High levels of PRAL were found to be related to an increased risk of diabetes in a cohort study in French females[34]. In the study by Akter et al[35], which was a cross-sectional investigation, researchers found that high levels of PRAL were related to the existence of insulin resistance. A study[36] carried out on Japanese patients reported that there was a link between the high PRAL score and risk of type 2 diabetes in men. According to the finding of a case-control study conducted by Hatami et al[33], a high dietary acid load can be linked an increased risk of type 2 diabetes. The study was conducted by Kiefte-de Jong et al[37], who evaluated the PRAL and NEAP estimates in 3 different cohorts (Nurse Health Study, Nurses Health Study II and Health Professionals Follow-Up Study), demonstrating that high diet-dependent acid load is associated with an increased risk of type 2 diabetes. A meta-analysis[38] that included four studies found that an increase in the risk of type 2 diabetes of 22% in patients with the highest PRAL and 23% for NEAP was estimated. This study is consistent with previous studies[33,34,37,38] and revealed that a high dietary acid load was associated with a higher risk of type 2 diabetes.

Dietary acid load and diabetes are linked through a few different mechanisms. Cortisol levels and glucocorticoid secretion both increase during metabolic acidosis; higher levels of cortisol can cause insulin resistance[39]. Adiponectin, which acts as an insulin sensitizer, is suppressed by metabolic acidosis and its levels in the blood are decreased. Low adiponectin levels are associated with increases in insulin resistance risk[40]. Magnesium and potassium, (which are found in plant-based foods) play an important role in maintaining that balance. Hence, diets that are deficient in fruit and vegetables shift the body's pH balance toward acidosis, which inhibits the beta-cell response. That, in turn, leads to insulin resistance[41]. A malfunction in renal ammonia synthesis or abnormalities in sodium, potassium, and hydrogen transport in the kidney tubules can cause decreased urine citrate excretion. Low urinary citrate excretion is most likely associated with insulin resistance[35,42]. Furthermore, an acidotic condition might affect insulin-like growth factor I (IGF-I), which can trigger insulin sensitivity as well as other complications[43].

Acid-base homeostasis is increasingly being recognized to play an important role in normal metabolic function[17]. Recent literature suggest that higher dietary acid load is associated with chronic low-grade metabolic acidosis and may increase the risk of insulin resistance and type 2 diabetes. The regulation of metabolic acid load appears to be important for metabolic health, and it may hold promise in the context of possible therapies to improve glycemic control in diabetic or insulin-resistant individuals. According to the findings, it is possible that improvement in dietary acid-base balance could be beneficial in the prevention of type 2 diabetes incidence. Future research is required to support the existing evidence and better elucidate the issue. If future studies confirm that reducing dietary acid load accompanies improving insulin sensitivity and reducing the risk of developing type 2 diabetes, this may lead to the development of more specific diet recommendations that results in metabolically favourable acid-base balance.

The present study has several strengths. First, a trained dietitian interviewed the participants to

obtain a 24-hour dietary recall and used the data from that to acquire their dietary acid levels *via* two methods (PRAL and NEAP). Second, the inclusion and exclusion criteria were quite stringent; the participants were disqualified if their regular diet was affected by issues connected to their health. Third, to our knowledge, this study was the first attempt to examine the correlation between dietary acid load and risk of developing type 2 diabetes in Turkish adults.

Limitations

However, it has some limitations. This study, like all other observational studies, is subject to the same methodological restrictions. Therefore, it is difficult to establish a causal connection between the dietary acid load and the risk of developing type 2 diabetes. In addition, acid-base levels in the body were measured according to calculations based on diet recall. When measurements of the pH of urine and serum are also available, the results will be more accurate. The present study focused solely on the effect that potential confounder variables had on the outcomes of adjusted models; however, there may be more residual variables that haven't yet been identified and could affect the results.

Conclusions

In conclusion, the findings of the current study suggested that an increase in the acid load of the diet would be associated with an increased risk of type 2 diabetes among Turkish people. This study indicates that improved balance may be an effective intervention strategy for preventing type 2 diabetes. It should be noted that this is only an observational study, and there is a need for interventional studies to assess whether changes in dietary acid load have an effect on the risk of type 2 diabetes.

Funding

This study received no external funding.

Authors' Contributions

Conceptualization, E.E.O.; methodology E.E.O.; formal analysis, E.E.O. and H.Y.; investigation, E.E.O. and H.Y.; resources; E.E.O. and H.Y; data curation, E.E.O. and H.Y.; writing-original draft preparation, E.E.O.; writing-review and editing, E.E.O. and H.Y. All authors read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki. Approval of the Ethics Committee of the Gaziantep Islam Science and Technology University (protocol 2022/120 approval date: 07.06.2022) was taken for the study.

Informed Consent

Informed consent was obtained from all the subjects participating in the study.

Data Availability

The datasets generated during and/or analyzed during the current study are not publicly available due privacy of patient data but are available from the corresponding author on reasonable request.

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