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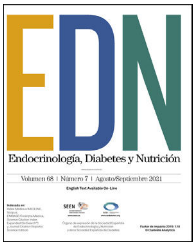

ORIGINAL ARTICLE

The effects of diet quality and dietary acid load on insulin resistance in overweight children and adolescents

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KEYWORDS
Adolescent;
Child;
Diet quality;
Dietary acid load;
Insulin resistance;
Overweight

Abstract
Introduction: This study aimed to investigate the association of diet quality (DQ) and dietary acid load (DAL) with insulin resistance (IR) in overweight children and adolescents.
Materials and methods: The study was conducted on 135 overweight participants aged 6–17 years. DQ was assessed using the Healthy Eating Index 2015 (HEI-2015) and the HEI-2015-TUBER, revised in accordance with the Turkey Dietary Guidelines (TUBER). Estimation of DAL was made calculating the potential renal acid load (PRAL) and net endogenous acid production (NEAP) scores.
Results: The HEI-2015-TUBER score was lower in those with IR than in those without IR ($p = 0.021$). Higher PRAL and NEAP scores were found in those with IR ($p = 0.060$ and $p = 0.044$, respectively). Moreover, a one-unit increase in the HEI-2015-TUBER score and the DAL score was associated with a reduction of 4.2% and a rise of approximately 3% in IR risk, respectively.
Conclusions: Healthy eating habits in overweight paediatric groups may help to reduce the IR risk, improving DQ and decreasing DAL.
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PALABRAS CLAVE
Adolescente;
Niño;
Calidad de la dieta;
Carga ácida de la dieta;

Los efectos de la calidad de la dieta y la carga ácida de la dieta sobre la resistencia a la insulina en niños y adolescentes con sobrepeso

Resumen
Introducción: Este estudio tuvo como objetivo investigar la asociación de la calidad de la dieta (CD) y la carga ácida de la dieta (CAD) con la resistencia a la insulina (RI) en niños y adolescentes con sobrepeso.

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Resistencia a la insulina;
Sobrepeso

Materiales y métodos: El estudio se realizó en 135 participantes con sobrepeso de entre 6-17 años. La CD se evaluó utilizando el índice de alimentación saludable (HEI)-2015 y el HEI-2015-TUBER, revisado de acuerdo con las Pautas Dietéticas de Turquía (TUBER). La estimación de la CAD se realizó calculando las puntuaciones de carga de ácido renal potencial (PRAL) y la producción neta de ácido endógeno (NEAP).

Resultados: La puntuación HEI-2015-TUBER fue más baja en aquellos con RI que en los que no tenían RI ($p = 0{,}021$). Se encontraron puntuaciones PRAL y NEAP más altas en aquellos con RI ($p = 0{,}060$ y $p = 0{,}044$, respectivamente). Además, un aumento de una unidad en la puntuación HEI-2015-TUBER y las puntuaciones de la CAD se asoció con una reducción del 4,2% y un aumento de aproximadamente el 3% en el riesgo de RI, respectivamente.

Conclusiones: Los hábitos alimenticios saludables en los grupos pediátricos con sobrepeso pueden ayudar a reducir el riesgo de RI mejorando la CD y disminuyendo la CAD.

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Introduction

In recent years, the increase in childhood obesity has become a major global public health problem.[1] It is known that approximately 110 million children and adolescents are overweight and obese worldwide.[2] Unhealthy eating habits, as well as excessive and unbalanced energy intake, have an effect on the emergence of obesity. Thus, a high quality diet plays an important role in the prevention and treatment of obesity.[3] Meanwhile, obesity occurring in children and adolescents is a major modifiable risk factor for insulin resistance (IR).[1] IR, seen in nearly half of obese children and adolescents, is associated with several metabolic disorders and is an important risk factor for the development of type 2 diabetes (T2D) and cardiovascular diseases in adulthood.[1,4] Therefore, it is important to know and treat the mechanisms that lead to IR.

The development of IR is determined by the nutritional habits, lifestyle, and physical activity status of the individuals. A healthy and balanced diet has been shown to improve glucose and insulin homeostasis.[5] For this reason, improving diet-related health problems and identifying and changing negative nutritional behaviours provide benefits in preventing the development of IR.[6] However, especially in children and adolescents, the consumption of unhealthy foods like refined sugar, sugary drinks, and fatty and salty foods increases with a shift to Western-style diets, while the consumption of healthy foods like vegetables, fruit and whole grains decreases. These dietary habits lead to imbalanced nutrient intake and a reduction in diet quality (DQ).[7] It is also known that such diets have a high dietary acid load (DAL) along with low DQ.[8] DAL causes metabolic changes and increases the prevalence of obesity as well as metabolic acidosis in children and adults.[9,10] Increased metabolic acidosis has been associated with high adiposity[11,12] and IR.[10] It has also been suggested that diets with high DAL may increase the risk of chronic diseases associated with IR.[10,13] Nevertheless, the relationship between DAL and IR in overweight children and adolescents has not yet been ascertained. Therefore, the aim of the current study is to determine the DQ and DAL of overweight children and adolescents and to evaluate the possible association of these parameters with IR.

Materials and methods

Study population

This cross-sectional study was conducted on 135 overweight children and adolescents aged 6–17 years, who attended the paediatric endocrinology outpatient clinic at the Erciyes University Children's Hospital. The exclusion criteria were having any health problems limiting their physical activity, and using tobacco, alcohol or any medications.

Ethical approval was obtained from the Clinical Research Ethics Committee of Erciyes University (reference code: 2010/133). Participants and their families were informed about the research in accordance with the Declaration of Helsinki, and then a written informed consent form was read and signed by the volunteers.

Anthropometric measurements

Participants' body weight and height were measured according to standard procedures by trained researchers. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Overweight (including obesity) was defined as having a BMI ≥ 85th percentile of Turkish growth reference data,[14] and children and adolescents with a BMI ≥ 85th percentile were recruited to this study. WHO Anthro Plus software (version 1.0.4) was used to calculate BMI *z*-scores. The tri-ponderal mass index (TMI, kg/m^3) was also calculated.

Clinical assessment

All participants were examined by the paediatric endocrinologist before the study. Blood glucose, insulin, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were measured after 12 h of fasting. The HOMA-

IR score, a valid tool for evaluating IR in children and adolescents,[15] was calculated, and 2.6 and 3.2 were used as the threshold to define IR for prepubertal and pubertal patients, respectively.[16]

Dietary assessment

A three-day dietary record was taken to evaluate the nutritional status of the participants. They were instructed on how to record diet diaries and were asked to record all foods and drinks (including water) consumed for three days (two weekdays and one weekend day). At the end of this period, the research dietician checked each dietary record and sought clarification about portion sizes using a photographic food atlas. Diet composition was analysed using the BeBiS Nutrition Information System software version 7.2.

Determining diet quality

The Healthy Eating Index 2015 (HEI-2015) score,[17] a measure for assessing dietary quality, was calculated using the dietary records. The highest score of HEI-2015 is 100, and it classifies dietary quality ≤ 50 as ''poor'', 51–80 as ''needs improvement'', and ≥ 80 as ''good''. The HEI-2015 was also revised in accordance with the Turkey Dietary Guidelines (TUBER) recommendations,[18] and the HEI-2015-TUBER scores were calculated.

Dietary acid load calculation

The DAL was calculated using potential renal acid load (PRAL) and net endogenous acid production (NEAP) algorithms.[19,20] The NEAP score includes protein and potassium as acidity-changing nutrients. The PRAL score estimates the DAL taking into account the intestinal absorption rates of protein and additional minerals taken with the diet. There are no cut-off points, higher PRAL and NEAP scores indicate that the acidic load has increased, while low values indicate that the alkali load has increased.

Statistical analyses

Sample size and power analysis: The statistical software G*Power (version 3.1) was used to calculate sample size and power. Considering 95% power and $\alpha = 0.05$, the minimum required sample size was 130 participants to detect a significant difference (effect size = 0.634) in the mean HOMA values between groups.[15] When the sample power was calculated for this study according to the difference between the means of groups obtained by the *t*-test in the HOMA-IR score, the sample size of 135 participants provided 99.9% power at an alpha level of 0.05.

Data analysis: Statistical analysis was performed using the IBM SPSS Statistics (version 22.0) software. Data were expressed as the number (*n*) and percentage (%) for categorical variables, and mean and 95% confidence intervals (CI) for continuous variables. Normality was assessed using the histogram, normal *Q–Q* plots and the Kolmogorov–Smirnov test. Two independent group comparisons were performed by the Student's *t*-test and Mann–Whitney *U* test for continuous variables with and without normal distributions, respectively. Categorical variables were compared by the chi-square test. In addition, logistic regression analyses were performed to determine the effect of DQ and DAL on IR. The non-IR category was considered the reference group, and age was controlled in the regression models. All potential confounding variables (age, gender, etc.) were considered separately using the univariate analysis, and any variables having a significant Wald test at a level of 0.25 were selected for the multivariate analysis.[21] Each potential confounder was also tested in the multivariate models and was retained as a confounding variable if it was significant and increased Nagelkerke R^2 values or modified the respective association substantially. Odds ratios (OR) with 95% CI were reported, and p values < 0.05 were considered statistically significant for all data.

Results

Participant characteristics

This study was conducted with 135 overweight children and adolescents (40% boys). In order to determine the effect of IR, the participants were divided into two groups: those with IR and those without IR. The age ($p < 0.001$) and TMI ($p = 0.001$) of the IR group were higher than the non-IR group, while their gender and BMI *z*-scores were similar ($p > 0.05$). Furthermore, serum triglyceride levels were higher ($p = 0.002$), and HDL-C levels were lower ($p = 0.003$) in the group with IR. No differences were found in total cholesterol and LDL-C ($p > 0.05$) (Table 1).

Dietary intake, DQ, and DAL

The average daily intake of energy, and macro- and micronutrients was similar between the IR and non-IR ($p > 0.05$) groups. However, the HEI-2015 score according to TUBER was lower in those with IR ($p = 0.021$). In the classification according to both the HEI-2015 and HEI-2015-TUBER scores, the rate of those with poor DQ was higher in the IR group ($p = 0.034$ and $p = 0.037$, respectively). In addition, the PRAL and NEAP scores, indicators of DAL, were higher in the group with IR, while this difference was statistically significant only for the NEAP scores ($p = 0.060$ and $p = 0.044$, respectively) (Table 2).

Associations of DQ and DAL with IR

When DQ, DAL and IR variables were modelled, significant associations were observed in the logistic regression analysis (Table 3). An increase in the HEI-2015-TUBER score was associated with a decrease of 4.2% in the risk of IR (OR 0.958, 95% CI 0.924, 0.994). Furthermore, greater PRAL (OR 1.033, 95% CI 1.000, 1.067) and NEAP (OR 1.025, 95% CI 1.001, 1.051) scores were associated with higher IR risk.

Discussion

Obesity is a critical risk factor in the development of IR in both paediatric and adult groups. It is known that IR

Table 1 Participants' characteristics and biochemical parameters.

Variables[a]	Non-IR ($n = 77$)	IR ($n = 58$)	p[*]
Gender (male), n (%)	30 (39)	24 (41)	0.776
Age (years)	10.82 (10.12, 11.51)	12.45 (11.87, 13.02)	<0.001
BMI-Z score (SD)	2.61 (2.44, 2.77)	2.80 (2.65, 2.95)	0.098
TMI (kg/m^3)[b]	17.93 (17.49, 18.36)	19.21 (18.59, 19.82)	0.001
Glucose (mg/dl)	84.91 (83.27, 86.55)	89.34 (87.11, 91.58)	0.001
Insulin (μU/ml)	9.76 (9.06, 10.46)	26.90 (23.06, 30.74)	<0.001[**]
HOMA-IR	2.05 (1.90, 2.19)	5.98 (5.05, 6.90)	<0.001[**]
Triglycerides (mg/dl)	101.93 (90.81, 113.06)	126.52 (113.22, 139.81)	0.002[**]
Total cholesterol (mg/dl)	175.13 (168.44, 181.82)	181.67 (174.24, 189.10)	0.195
HDL-C (mg/dl)	46.77 (44.19, 49.35)	41.56 (39.15, 43.97)	0.003[**]
LDL-C (mg/dl)	108.38 (102.81, 113.95)	116.52 (108.44, 124.59)	0.090

Abbreviations: BMI, body mass index; HDL-C, high density lipoprotein cholesterol; IR, insulin resistance; LDL-C, low density lipoprotein cholesterol; TMI, tri-ponderal mass index.

[a] Values were given as mean and 95% confidence interval unless otherwise indicated.

[b] Children less than 8 years old were excluded from the analysis.

[*] Student's t-test.

[**] Mann–Whitney U test.

Table 2 Participants' energy and nutrient intakes, diet quality and dietary acid load.

Variables[a]	Non-IR ($n = 77$)	IR ($n = 58$)	p[*]
Energy (kcal)	1874.63 (1752.65, 1996.61)	1946.81 (1806.24, 2087.38)	0.440
Carbohydrates (%)	50.27 (48.94, 51.60)	51.30 (49.55, 53.04)	0.343
Proteins (%)	13.89 (13.37, 14.42)	13.83 (13.21, 14.45)	0.875
Fats (%)	35.84 (34.74, 36.94)	34.92 (33.33, 36.51)	0.327
Vitamin B_1 (mg/1000 kcal)	0.81 (0.75, 0.88)	0.78 (0.72, 0.85)	0.488
Vitamin B_2 (mg/1000 kcal)	1.26 (1.17, 1.34)	1.23 (1.12, 1.34)	0.716
Vitamin B_6 (mg/1000 kcal)	1.26 (1.11, 1.41)	1.20 (1.11, 1.29)	0.906[**]
Folic Acid (mcg/1000 kcal)	257.95 (238.35, 277.54)	257.64 (235.68, 279.59)	0.983
Vitamin B_{12} (mcg/1000 kcal)	3.86 (3.35, 4.37)	3.54 (2.90, 4.18)	0.268[**]
Vitamin E (mg/1000 kcal)	18.67 (16.90, 20.43)	18.43 (16.37, 20.48)	0.773[**]
Vitamin C (mg/1000 kcal)	104.07 (92.95, 115.19)	100.28 (87.27, 113.29)	0.594[**]
Calcium (mg/1000 kcal)	676.23 (621.51, 730.96)	666.58 (597.79, 735.38)	0.825
Magnesium (mg/1000 kcal)	236.90 (219.36, 254.45)	229.77 (210.57, 248.98)	0.588
Iron (mg/1000 kcal)	10.29 (9.60, 10.98)	10.56 (9.92, 11.20)	0.585
Zinc (mg/1000 kcal)	8.84 (8.25, 9.44)	8.98 (8.27, 9.70)	0.766
HEI-2015 score	47.87 (45.86, 49.87)	45.63 (43.65, 47.62)	0.124
HEI-2015 score classification (poor), n (%)	42 (54)	42 (72)	0.034
HEI-2015-TUBER score	38.69 (36.29, 41.10)	34.61 (32.18, 37.04)	0.021
HEI-2015-TUBER score classification (poor), n (%)	64 (83)	55 (95)	0.037
PRAL (mEq/day)	8.68 (6.17, 11.19)	12.49 (9.30, 15.67)	0.060
NEAP (mEq/day)	53.02 (49.77, 56.28)	58.33 (54.16, 62.49)	0.044

Abbreviations: HEI, healthy eating index; IR, insulin resistance; PRAL, potential renal acid load; NEAP, net endogenous acid production; TUBER, Turkey Dietary Guidelines.

[a] Values were given as mean and 95% confidence interval unless otherwise indicated.

[*] Student's t-test.

[**] Mann–Whitney U test.

increases the risk of T2D and cardiovascular disease associated with overweight. IR is also an important component of metabolic syndrome, and its incidence is increasing, especially among obese children and adolescents.[1,22] On the other hand, the eating habits of individuals may affect IR and the development of related complications.[23] Therefore, determining the effects of DQ and DAL on IR may be useful for its prevention and treatment. Our study aimed to determine the relationship of DQ and DAL with IR in overweight children and adolescents. The present findings showed that DQ was lower and DAL was higher in those with IR. Additionally, an increase in DQ scores decreased the risk of IR, while

Table 3 Association of dietary acid load and diet quality scores with risk of insulin resistance.

Variables[a]	IR OR (95% CI)	p
HEI-2015 score	0.964 (0.922, 1.007)	0.099*
HEI-2015-TUBER score	0.958 (0.924, 0.994)	0.023*
PRAL (mEq/day)	1.033 (1.000, 1.067)	0.047*
NEAP (mEq/day)	1.025 (1.001, 1.051)	0.045*

Abbreviations: HEI, healthy eating index; IR, insulin resistance; PRAL, potential renal acid load; NEAP, net endogenous acid production; TUBER, Turkey Dietary Guidelines.

[a] Values are odds ratio (95% confidence interval) estimated through logistic regression using the non-IR group as reference. All models were adjusted for age.

* p-for trend < 0.01.

increased DAL scores were related to higher IR risk. Considering the importance of preventing the risk of developing IR in childhood obesity, these findings may guide the development of different strategies to improve the nutritional status of children.

Insulin resistance is a clinical condition in which the body's response to insulin is inadequate and glucose homeostasis cannot be provided effectively.[24] Studies have emphasised that children with IR are more prone to developing T2D, metabolic syndrome and cardiovascular disease in the future.[25–27] Greater IR incidence is observed among overweight/obese individuals[28,29] and a 4.5 fold increased HOMA-IR score was recorded in adolescents with higher body fat percentages.[30] For this reason, the use of appropriate and economical screening tools to determine body fat percentage in childhood may provide effective interventions. Although BMI is widely used, it fails in some clinical evaluations because it cannot distinguish between fat and lean mass in the body.[31] Peterson et al.[25] suggested that a new method, the TMI, predicts fat mass better. TMI has also been suggested as an appropriate method for preventing cardiometabolic comorbidities and evaluating adiposity.[32] In line with the literature, in our study, TMI was found to be higher in participants with IR even though there was no difference in BMI between those with IR and those without IR. Therefore, the use of TMI may be beneficial in patients more than 8 years old. Furthermore, since the evaluation of TMI in children is not dependent of age and puberty, its use in the clinic may be more advantageous.[31,32]

Obese children and adolescents with IR tend to have a worse metabolic profile than those without IR,[29] and higher serum triglyceride levels, lower HDL-C levels and a positive correlation of TG/HDL-C ratio with the HOMA-IR index have been reported.[33] Similarly, the present study showed that children and adolescents with IR have higher serum triglyceride levels and lower HDL-C levels. Excess energy intake and a sedentary lifestyle a cause greater waist circumference and fatty liver with a rise in body fat in obese individuals. Consequently, more IR and pro-inflammatory cytokine production are observed. This adverse profile results in increased plasma glucose, triglyceride and blood pressure, and decreased HDL-C level.[34]

It is known that the consumption of fruit, vegetables and whole-grain foods that enhance DQ in obese individuals is protective against the risk of impaired glucose metabolism and the development of T2D.[35] Therefore, there is an increasing relevance in DQ to describe the relationship between childhood obesity and nutrition in the literature.[22,36] High-energy, high-fat and low-dietary fibre dietary habits that reduce DQ in childhood and adolescence were reported as associated with a higher risk of obesity.[37] Additionally, the DQ of obese children was found to be poor,[38] and an increase in DQ scores was related to a reduced risk of IR.[22] Consistent with the literature, our results showed that DQ was lower, and the rate of those with poor DQ was higher in overweight children and adolescents with IR compared to those without IR. Furthermore, a one-unit increase in the HEI-2015-TUBER score was found to be associated with a reduction of 4.2% in IR risk. While consumption of vegetables, fruit and whole grains is generally inadequate in this age group, the energy, saturated fat and sodium intake increase, especially due to the high consumption of processed and packaged foods, which leads to poor DQ.[37,39] Given that compliance with healthy eating habits is efficient in reducing IR in overweight individuals, paying attention to DQ during childhood and adolescence may help to decrease the risk of developing comorbidities and chronic diseases in later life.

Western-style diets with a poor DQ cause higher DAL and increase the risk of metabolic disorders, as they contain more animal protein (red meat, processed meat products, etc.) and less fruit and vegetables.[8,9,40] Acid-base balance is important in the development of metabolic disorders,[11] and it has been asserted that metabolic acidosis caused by rising DAL may increase IR.[40,41] In a recent study, DAL, reflected by PRAL and NEAP scores, has been determined to associate positively with IR risk in obese adults.[41] However, no studies on paediatric groups have been found in the literature. To our knowledge, this is the first research conducted on children and adolescents. In line with the adult study, the present findings indicated that obese individuals with IR had higher PRAL and NEAP scores than those without IR, and a one-unit increase in DAL scores was related to a rise of approximately 3% in IR risk. Although the mechanisms of the relationships between diet-induced metabolic acidosis and IR remain unclear, there are various possible explanations. Firstly, low blood pH could disrupt insulin binding to its receptors, leading to IR. Another mechanism is that metabolic acidosis stimulates the secretion of cortisol and suppresses adiponectin gene expression. Chronically elevated cortisol levels and/or low adiponectin levels may induce IR.[41]

This study had some limitations. First, a healthy control group was not included in our study. Therefore, the relationship between obesity and DQ or DAL could not be revealed. Second, there was no detailed information about the lifestyle habits of participants, such as their physical activity. Considering the effect of energy expenditure, which plays an important role in the development of obesity, associations between lifestyle factors and IR could not be determined. However, the present study is the first to assess the relationship between DAL, as well as DQ, and IR in overweight children and adolescents. Our findings showed that although energy and nutrient intakes of those with IR and those without IR were similar, high DAL and/or low DQ scores were associated with an increased risk of IR. These results indicate that for the prevention and treatment of IR in obese children and adolescents, it may not be sufficient to control daily energy and nutrient intake and that the quality of diet should also be improved.

In conclusion, in contrast to Western-style diets, adequate and balanced nutrition in overweight children is of great importance for both improving DQ and reducing DAL. Thus, by reducing the risk of IR it will be possible to contribute to both the improvement of metabolic control and the prevention of metabolic syndrome and cardiovascular diseases. Therefore, it would be beneficial to provide nutritional education to children and adolescents on the consumption of healthy foods such as vegetables, fruit and whole grains, instead of foods containing high energy, saturated fat, sugar and salt to help them acquire appropriate dietary habits. Moreover, well-planned and long-term studies are needed to clarify the relationship of DQ and DAL with IR in overweight children and adolescents.

Authors' contributions

Z.C. designed the research protocol, conducted the research and statistical analysis, prepared the manuscript, and had primary responsibility for the final content. B.E. contributed to the data analysis and manuscript writing. N.H. and S.K. contributed to the planning and management of the study and the data collection, and reviewed the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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