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Predictive Value of the Adiponectin-to-Leptin Ratio for Insulin Resistance and Cardiometabolic Risk in Obese Children and Adolescents aged 10–18 years

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Abstrak. Childhood obesity is increasingly associated with early cardiometabolic problems and insulin resistance. The adipokine ratio may be a better indicator of metabolic dysfunction than either adipokine alone since both leptin and adiponectin are hormone agents that are generated by fat and have distinct metabolic activities. This research sought to determine if the adiponectin-to-leptin ratio (ALR) might predict insulin resistance and cardiometabolic risk in obese children and adolescents. This descriptive cross-sectional analytical research was conducted at Tikrit Teaching Hospital between February 2024 and February 2025. Fifty kids of comparable age and gender and fifteen obese kids and teenagers (10–18 years old). Following an overnight fast, anthropometric and clinical parameters were assessed, and blood samples were taken to evaluate glucose, insulin, adiponectin, leptin, lipid profile, and high sensitivity C-reactive protein. The HOMA-IR was used to measure insulin resistance, and the ratio of serum adiponectin to leptin was used to measure ALR. Receiver operating characteristic analysis, multivariable regression analysis, and correlation analysis were performed. Adiponectin and ALR values were substantially lower in the obese individuals compared to the control group ($P < 0.001$), whereas BMI, WC, fasting insulin levels, HOMA-IR, leptin, triglycerides, LDL-C, blood pressure, and hs-CRP values were significantly higher. ALR was an independent predictor of insulin resistance and had a negative correlation with HOMA-IR ($r = -0.61$, $P < 0.001$). With an AUC of 0.86, a sensitivity of 82.0%, a specificity of 78.7%, and an ideal cut-off of ≤0.28, ALR was shown to be the greatest predictor of insulin resistance based on ROC analysis. Additionally, ALR predicted significant cardiometabolic risk with a high AUC of 0.82. In obese children and adolescents, the adiponectin-to-leptin ratio has a substantial correlation with insulin resistance and cardiometabolic disorders. It may be a valuable biomarker for identifying children who are at increased metabolic risk.

Keywords: Adiponectin; Leptin; Adiponectin-to-leptin ratio; Insulin resistance; Childhood obesity.

1. Introduction

Due to its association with insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, and cardiovascular disease in adulthood, childhood and adolescent obesity has become a significant public health concern [1], [2]. One major metabolic consequence of pediatric obesity is insulin resistance, which also serves as a critical bridge between high adiposity and potential cardiometabolic health problems. Children who are obese have reduced insulin action due to a number of causes, including elevated levels of free fatty acids, altered lipid metabolism, inflammation, and aberrant levels of endocrine signals from adipose tissue [2], [3].

Adipose tissue, an active endocrine organ, secretes this network of physiologically active chemicals known as adipokines. These mediators have a role in vascular function, inflammation, energy balance, and the metabolism of fats and carbohydrates. Obesity causes substantial alterations in the synthesis of adipokines, and the general expression pattern is pro-inflammatory and metabolically pro-inflammatory [4]. Since metabolic problems may arise even prior to the development of diabetes and/or cardiovascular disease, this adipose tissue malfunction is particularly significant in children [5].

Adiponectin, which has many insulin-sensitizing, anti-inflammatory, and metabolic functions, is one of the most prevalent hormones released by adipocytes. Adiponectin levels have been connected to insulin resistance and metabolic dysfunction and are generally negatively correlated with body fat [6]. On the other hand, leptin levels increase in direct proportion to fat accumulation and are involved in neuroendocrine signaling, hunger, and energy expenditure. The hormone leptin normally correlates with the amount of stored body fat, but elevated leptin levels in obese people may lead to leptin resistance and detrimental metabolic consequences [7].

Adiponectin and leptin's opposing functions imply that their combination may provide more information than each one alone. As a result, the adiponectin/leptin ratio (ALR) has emerged as a potentially useful indicator of metabolic imbalance and adipose tissue malfunction. As a measure of metabolic risk, the adiponectin/leptin ratio has previously been shown to predict insulin resistance and metabolic syndrome characteristics in obese children [8]. Additionally, some studies have shown that changes in adipokines in the pediatric population may be a precursor to clinically evident metabolic disorder and are linked to anomalies of glucose and lipid metabolism [9].

Clinically meaningful biomarkers are needed to identify obese children who are more likely to develop insulin resistance and cardiometabolic disorders, despite the growing body of information regarding the function of adipokines in pediatric obesity. In this sense, the ALR may be useful since it combines a physiologically protective adipokine with a hormone linked to obesity, and it may provide a more precise picture of the degree of adipose tissue malfunction than anthropometric measurements alone. Therefore, the goal of the current research was to evaluate the predictive value of the adiponectin/leptin ratio for insulin resistance and cardiometabolic risk in obese children and adolescents (ages 10 to 18).

2. Research Methodology

Study Design and Setting

In hospital-based analytical cross-sectional research, the goal was to evaluate the predictive value of the adiponectin to leptin ratio (ALR) for insulin resistance and cardiometabolic risk in obese children and adolescents. The current research was carried out during a 12-month period, from February 2024 to February 2025, at the Tikrit Teaching Hospital in the Salah Al-Din Governorate in Iraq. Children and teenagers (10–18 years old) who visited the pediatric outpatient clinic and were diagnosed with obesity based on age- and sex-specific BMI-for-age categorization were included in this research. The school-age and teenage years, when metabolic problems and insulin resistance linked to obesity begin to become more noticeable, were included in the age range selected. According to the WHO 2007 growth reference, individuals between the ages of 10 and 18 who had a BMI-for-age more than +2 standard deviations from the age- and sex-specific median were considered obese.

Study Population and Sample Size

150 obese children and adolescents between the ages of 10 and 18 were recruited using a sequential sampling technique. Patients who were within the designated age range, had obesity as determined by the BMI-for-age criteria, and had not taken any medications known to have a substantial impact on glucose or lipid metabolism were included in the research. Children with endocrine disorders brought on by obesity, acute or chronic inflammatory diseases, genetic syndromes, diabetes mellitus, congenital or acquired heart disease, chronic kidney or liver disease, or those presently receiving corticosteroid or lipid-lowering therapy were not included. Additionally, children with inadequate biochemical or anthropometric data were not included. A group of fifty children and adolescents who seemed to be in good health and had a normal BMI for their age was also enlisted as a reference control group so that adipokines and metabolic parameters could be compared.

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The Anthropometric and Clinical Evaluation

Every participant had a conventional anthropometric assessment. A calibrated weighing scale (0.1 kg) was used to determine the body weight when the subject was wearing light clothes and no shoes. A stadiometer that was fixed to a wall was used to measure height to the closest 0.1 cm. Z-scores for BMI-for-age were calculated using the age- and sex-specific WHO growth guidelines [10]. BMI was calculated by dividing weight (kg) by height (m^2). Using a non-stretchable measuring tape, the waist circumference was measured halfway between the top border of the iliac crest and the lowest rib at the conclusion of a typical expiration. WHR was calculated after the hip circumference was measured at the buttocks' broadest point. An suitably sized cuff and a calibrated automated sphygmomanometer were used to measure seated blood pressure after at least five minutes of rest. The average score was obtained after two measurements were made within five minutes of one another. Systolic and diastolic blood pressure, resting heart rate, BMI, BMI-for-age Z score, waist circumference, and waist-to-height index were the primary clinical and anthropometric parameters.

Blood Sample Collection and Biochemical Analysis

About 8–10 mL of venous blood were taken from each individual in the morning while they were fasting for 8–12 hours under aseptic settings. Samples of blood were drawn into appropriate plain and anticoagulant tubes. After centrifuging the serum for ten minutes at around 3000 rpm, it was kept at -20°C for biochemical analysis. An enzymatic colorimetric technique and a commercially available enzyme-linked immunosorbent assay (ELISA) kit were used to measure the amount of circulating blood glucose and insulin in a sample's fasting serum. The homeostatic model assessment of insulin resistance (HOMA-IR), which uses the formula fasting insulin (µIU/mL) x fasting glucose (mmol/L) / 22.5, was used to measure insulin resistance.

Adipokine and Metabolic Measurements

Following the manufacturer's instructions, commercially available quantitative ELISA kits were used to measure the amounts of leptin and adiponectin in the serum. The blood levels of adiponectin and leptin from the same person were divided to get the adiponectin/leptin ratio. Using an automated clinical chemistry analyzer, the enzymatic colorimetric technique was used to measure the blood lipid parameters, including total cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Using an immunoturbidimetric technique, high-sensitivity C-reactive protein (hs-CRP) was also identified as a cardiometabolic risk marker of inflammation.

The primary laboratory measurements were fasting glucose, adiponectin, HOMA-IR, leptin, adiponectin/leptin, total cholesterol, triglyceride, HDL-C, LDL-C, and hs-CRP. Systolic and diastolic blood pressure, waist circumference, waist to height ratio, triglycerides, HDL-C, LDL-C, and hs-CRP were the main cardiometabolic markers. In particular, the research looked at how lower ALR was associated with higher HOMA-IR and worse cardiometabolic risk factors.

Assessment of Insulin Resistance and Cardiometabolic Risk

In addition to being categorized using an age-specific pediatric HOMA-IR threshold based on the research population or predetermined pediatric criteria, insulin resistance was primarily evaluated as a continuous metabolic outcome, HOMA-IR. A composite profile of cardiometabolic risk was created using central obesity, high blood pressure, hypertriglyceridemia, decreased HDL-C, raised LDL-C, and elevated hs-CRP. To determine the total estimate of cardiometabolic load, the number of unfavorable cardiometabolic components was recorded for each participant. The primary end measures were the cardiometabolic risk profile and HOMA-IR, with the ALR serving as the primary predictor variable.

Statistical Analysis

IBM SPSS Statistics version 23 was used for data entry, coding, and analysis. For continuous variables, which were shown as mean ± standard deviation and median with interquartile range based on the data distribution, the Shapiro-Wilk test and normality test were used; for categorical variables, these were displayed as frequencies and percentages. The independent-samples t-test and the Mann-Whitney U test were used to compare continuous variables between two and more groups, respectively. The Pearson or Spearman correlation coefficient was used to correlate ALR with anthropometric, biochemical, insulin resistance, and cardiometabolic data. After controlling for age, sex, waist circumference, BMI-for-age Z score, and other relevant metabolic characteristics, multiple linear regression was used to determine if ALR independently predicted HOMA-IR. Binary logistic regression was used to evaluate the independent predictive value of ALR for insulin resistance and high cardiometabolic risk. The optimal cutoff value for ALR to predict insulin resistance and cardiometabolic risk was determined using the receiver operating characteristic (ROC) curve analysis, and its area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. Statistical significance was defined as a two-tailed p-value of less than 0.05.

Ethical Considerations

The Declaration of Helsinki's ethical guidelines were followed for conducting the research procedure. The relevant institutional research ethics committee gave its ethical clearance before the study began. Children and adolescents (where applicable) and parents/legal guardians provided informed written permission to take part. Parents and legal guardians, as well as children and teenagers (where applicable), provided informed written permission. Participants' information was all anonymized and utilized only for research.

3. Result and Discussion

Result

Demographic and Clinical Characteristics of the Study Participants

The study involved 200 children and adolescents (150 obese and 50 apparently healthy, age and sex matched). The mean age of the obese group was 14.1 ± 2.2 years, compared to 13.8 ± 2.3 years for the control group, with no significant difference between the groups. The male proportion of the obese group was 54.0% and in the control group 52.0%. The obese group had significantly higher body weight, BMI, BMI-for-age Z-score, waist circumference, waist-to-height ratio, systolic BP and diastolic BP than the control group (all at $P < 0.001$) (Table 1).

Table 1. Demographic, Anthropometric, and Clinical Characteristics of Obese Participants and Controls

Parameter	Obese group (n=150)	Control group (n=50)	P-value
Age (years)	14.1 ± 2.2	13.8 ± 2.3	0.421
Male sex, n (%)	81 (54.0)	26 (52.0)	0.812
Female sex, n (%)	69 (46.0)	24 (48.0)	0.812
Weight (kg)	78.6 ± 17.4	48.9 ± 11.2	<0.001
Height (cm)	162.7 ± 10.8	159.8 ± 11.1	0.103
BMI (kg/m²)	29.5 ± 4.2	19.1 ± 2.4	<0.001
BMI-for-age Z-score	2.42 ± 0.39	0.21 ± 0.71	<0.001
Waist circumference (cm)	94.8 ± 11.6	67.9 ± 8.2	<0.001
Waist-to-height ratio	0.58 ± 0.06	0.43 ± 0.04	<0.001
Systolic BP (mmHg)	119.4 ± 11.8	105.7 ± 8.6	<0.001
Diastolic BP (mmHg)	75.2 ± 8.3	67.4 ± 6.9	<0.001
Resting heart rate (beats/min)	86.7 ± 10.2	79.8 ± 8.7	<0.001

Distribution of Obesity According to Age and Sex

The age groups 14-16 (48.0%) and 17-18 (30.0%) had the highest proportions of the 150 obese children, with the remaining proportion of 22.0% being 10-13 years old. There was a relative evenness in male to female ratio with a slight male predominance. The results of the analysis shows that there was no statistically significant relationship between sex and age category (P = 0.684) (Table 2).

Table 2. Age and Sex Distribution of the Obese Study Group

Age group	Male, n (%)	Female, n (%)	Total, n (%)
10–13 years	18 (22.2)	15 (21.7)	33 (22.0)
14–16 years	39 (48.1)	33 (47.8)	72 (48.0)
17–18 years	24 (29.7)	21 (30.5)	45 (30.0)
Total	**81 (100)**	**69 (100)**	**150 (100)**

P = 0.684.

Comparison of Fasting Glucose, Insulin, HOMA-IR, and Adipokines

There was no overlap in the fasting glucose and fasting insulin concentrations between obese and control participants. The mean HOMA-IR was about three times higher in the obese participants. Leptin was significantly higher, and adiponectin significantly lower, in the obese group. Table 3 shows that the adiponectin-to-leptin ratio was considerably lower in the obese participants than in controls (0.31 ± 0.18 vs. 1.42 ± 0.71, respectively; P < 0.001).

Table 3. Comparison of Glycemic Parameters and Adipokines Between Obese Participants and Controls

Parameter	Obese group (n=150)	Control group (n=50)	P-value
Fasting glucose (mg/dL)	96.8 ± 10.9	87.5 ± 7.4	<0.001
Fasting insulin (µIU/mL)	18.7 ± 9.6	7.1 ± 3.1	<0.001
HOMA-IR	4.46 ± 2.51	1.54 ± 0.72	<0.001
Adiponectin (µg/mL)	7.62 ± 3.18	12.91 ± 4.21	<0.001
Leptin (ng/mL)	25.4 ± 12.7	9.14 ± 4.52	<0.001
Adiponectin/leptin ratio	0.31 ± 0.18	1.42 ± 0.71	<0.001

Lipid Profile and hs-CRP

Results showed significant difference in the lipid profile of the two groups. Participants who were obese had significantly higher levels of total cholesterol, triglycerides and LDL-C and lower levels of HDL-C than the controls. In addition, hs-CRP concentrations were significantly higher among obese participants, indicating an increased inflammatory burden associated with obesity. The results are presented in Table 4.

Table 4. Lipid Profile and hs-CRP Levels in Obese Participants and Controls

Parameter	Obese group (n=150)	Control group (n=50)	P-value
Total cholesterol (mg/dL)	181.6 ± 32.4	154.8 ± 24.7	<0.001
Triglycerides (mg/dL)	146.7 ± 54.3	91.6 ± 25.8	<0.001
HDL-C (mg/dL)	40.8 ± 7.1	51.7 ± 8.2	<0.001
LDL-C (mg/dL)	111.4 ± 28.7	84.9 ± 21.5	<0.001
hs-CRP (mg/L)	3.21 ± 2.18	1.02 ± 0.71	<0.001

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein.

Prevalence of Insulin Resistance Among Obese Participants

Out of 150 obese individuals, 61 (40.7%) had insulin resistance and 89 (59.3%) had insulin sensitivity based on the predetermined insulin resistant criteria of HOMA-IR. BMI, WC, WHtR, SBP, DBP, fasting insulin, triglycerides, LDL-C, and hs-CRP were significantly higher in participants with insulin resistance. HDL-C and adiponectin levels were significantly decreased in the insulin-resistant subgroup (Table 5), in contrast.

Table 5. Clinical and Biochemical Characteristics of Obese Participants According to Insulin Resistance Status

Parameter	Insulin-resistant (n=61)	Insulin-sensitive (n=89)	P-value
Age (years)	14.3 ± 2.1	14.0 ± 2.3	0.421
BMI (kg/m²)	31.0 ± 4.0	28.5 ± 3.9	<0.001
BMI-for-age Z-score	2.58 ± 0.34	2.31 ± 0.39	<0.001
Waist circumference (cm)	99.2 ± 10.8	91.8 ± 10.7	<0.001
Waist-to-height ratio	0.61 ± 0.05	0.56 ± 0.05	<0.001
Systolic BP (mmHg)	123.4 ± 11.5	116.6 ± 10.8	<0.001
Fasting glucose (mg/dL)	101.2 ± 10.4	93.8 ± 9.7	<0.001
Fasting insulin (µIU/mL)	25.9 ± 8.8	13.8 ± 5.1	<0.001
HOMA-IR	5.91 ± 2.24	3.47 ± 1.28	<0.001
Adiponectin (µg/mL)	5.81 ± 2.41	8.86 ± 3.15	<0.001
Leptin (ng/mL)	31.6 ± 12.5	21.2 ± 10.9	<0.001
Adiponectin/leptin ratio	0.20 ± 0.09	0.39 ± 0.19	<0.001
Triglycerides (mg/dL)	168.5 ± 58.4	131.8 ± 46.7	<0.001
HDL-C (mg/dL)	37.9 ± 6.4	42.8 ± 6.9	<0.001
LDL-C (mg/dL)	119.8 ± 29.4	105.6 ± 26.2	0.002
hs-CRP (mg/L)	4.18 ± 2.31	2.55 ± 1.84	<0.001

Cardiometabolic Risk Components

Individual cardiometabolic risk factors were more common in the obese subjects who had insulin resistance. Overall, 58 patients (38.7%) had 3 or more adverse cardiometabolic parameters; these were considered to represent a high cardiometabolic risk profile. These components are summarized in Table 6.

Table 6. Distribution of Cardiometabolic Risk Components Among Obese Participants

Cardiometabolic component	n	%
Central adiposity	109	72.7
Elevated triglycerides	67	44.7
Reduced HDL-C	62	41.3
Elevated blood pressure	49	32.7
Elevated LDL-C	43	28.7
Elevated hs-CRP	71	47.3
≥1 risk component	132	88.0
≥2 risk components	91	60.7
≥3 risk components	58	38.7

Adiponectin-to-Leptin Ratio According to Cardiometabolic Risk Burden

The adiponectin/leptin ratio decreased with every incremental increase in the cardiometabolic risk burden. The mean ALR was highest among participants who had no major cardiometabolic abnormalities, and lowest among those with three or more risk components. This difference between risk categories was statistically significant ($P < 0.001$), as illustrated in Figure 1.

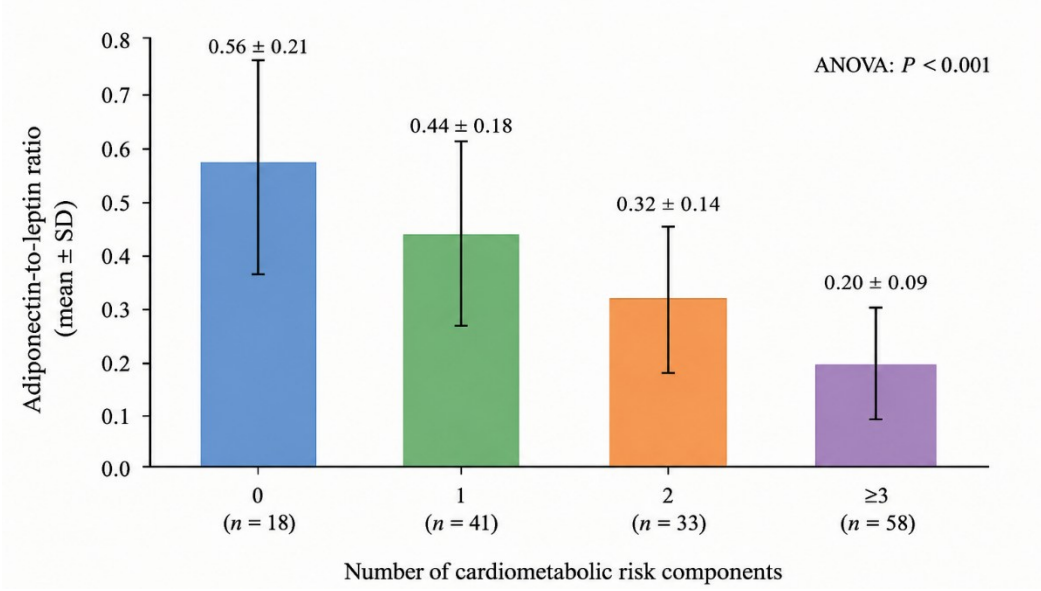

Figure 1. Progressive decline in the adiponectin-to-leptin ratio with increasing cardiometabolic risk burden.

Correlation Between Adiponectin-to-Leptin Ratio and Metabolic Parameters

A significant inverse correlation between ALR and HOMA-IR was found by correlation analysis ($r = -0.61$, $P < 0.001$) (Fig. 2). ALR was also inversely associated with BMI, BMI-for-age Z score, waist circumference, waist-to-height ratio, fasting insulin, triglycerides, LDL-C, systolic blood pressure and hs-CRP. However, a strong positive correlation was noted between ALR and HDL-C. The results for lower ALR were significantly correlated with increased adiposity, insulin resistance, dyslipidemia, inflammation and cardiometabolic burden (Table 7).

Table 7. Correlations Between Adiponectin-to-Leptin Ratio and Anthropometric, Glycemic, and Cardiometabolic Parameters

Parameter	Correlation coefficient (r)	P-value
BMI	−0.48	<0.001
BMI-for-age Z-score	−0.51	<0.001
Waist circumference	−0.55	<0.001
Waist-to-height ratio	−0.58	<0.001
Systolic BP	−0.36	<0.001
Diastolic BP	−0.29	<0.001
Fasting glucose	−0.34	<0.001
Fasting insulin	−0.57	<0.001
HOMA-IR	**−0.61**	**<0.001**
Triglycerides	−0.43	<0.001
HDL-C	**0.39**	**<0.001**
LDL-C	−0.31	<0.001
hs-CRP	−0.46	<0.001

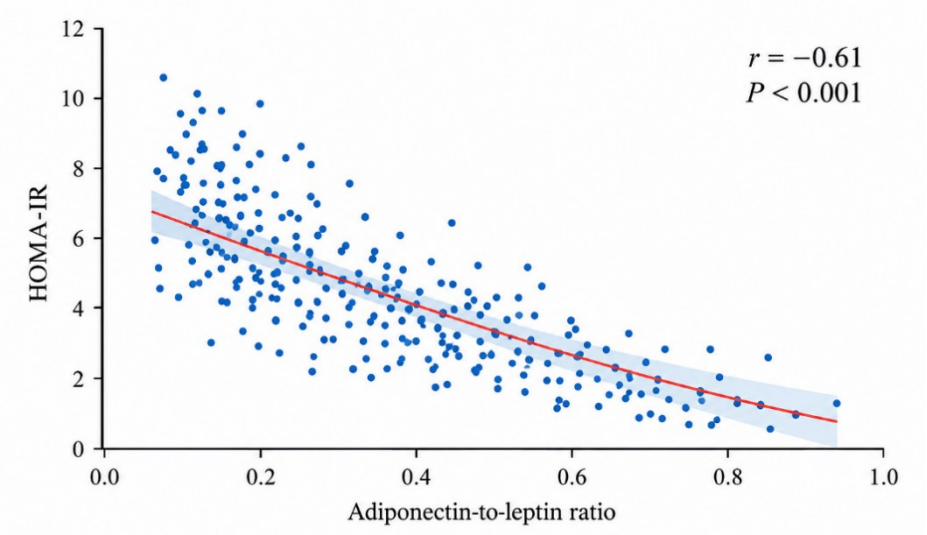

Figure 2. Scatter plot demonstrating the inverse correlation between adiponectin-to-leptin ratio and HOMA-IR.

Multiple Linear Regression Analysis for Predictors of HOMA-IR

Multiple linear regression analysis was used to see if the relationship between ALR and insulin resistance remained significant when other potential confounding variables were taken into account. The model showed that ALR was an independent inverse predictor of HOMA-IR. BMI-for-age Z score and waist circumference and fasting triglycerides were also independent positive predictors of HOMA-IR. The model accounted for about 48% of the variance in HOMA-IR (adjusted $R^2 = 0.48$) (Table 8).

Table 8. Multiple Linear Regression Analysis of Independent Predictors of HOMA-IR

Predictor	β coefficient	Standard error	P-value
Age	0.06	0.08	0.318
Male sex	0.04	0.17	0.527
BMI-for-age Z-score	0.29	0.11	<0.001
Waist circumference	0.21	0.07	0.003
Triglycerides	0.17	0.04	0.011
HDL-C	−0.09	0.05	0.146
hs-CRP	0.10	0.06	0.081
Adiponectin/leptin ratio	**−0.46**	**0.12**	**<0.001**

Model adjusted $R^2 = 0.48$; $P < 0.001$.

Logistic Regression Analysis for Insulin Resistance

A lower ALR was independently associated with higher odds of insulin resistance even after accounting for age, sex, BMI-for-age Z score, waist circumference and triglyceride concentration (P<0.001). The participants who had lower ALR values ran about four times greater risk for insulin resistance. Furthermore, WC and BMI-for-age Z score were still found to be significant independent predictors (Table 9).

Table 9. Multivariable Logistic Regression for Predictors of Insulin Resistance

Variable	Adjusted OR	95% CI	P-value
Age	1.08	0.91–1.28	0.381
Male sex	1.16	0.59–2.29	0.662
BMI-for-age Z-score	1.82	1.20–2.76	0.005
Waist circumference	1.04	1.01–1.07	0.009
Triglycerides	1.01	1.00–1.02	0.031
Lower adiponectin/leptin ratio	**4.37**	**2.12–9.01**	**<0.001**

Predictive Value of the Adiponectin-to-Leptin Ratio for Insulin Resistance

The adiponectin-to-leptin ratio showed good discrimination for detecting the insulin resistance within obese subjects, by ROC curve analysis. The area under the curve was 0.86 (95% CI: 0.80–0.91; P < 0.001). The best compromise of sensitivity and specificity was obtained with an ALR of ≤0.28 which yielded a sensitivity of 82.0% and a specificity of 78.7%. Positive PPV was 73.5% and the negative PPV was 85.5% (Fig. 3).

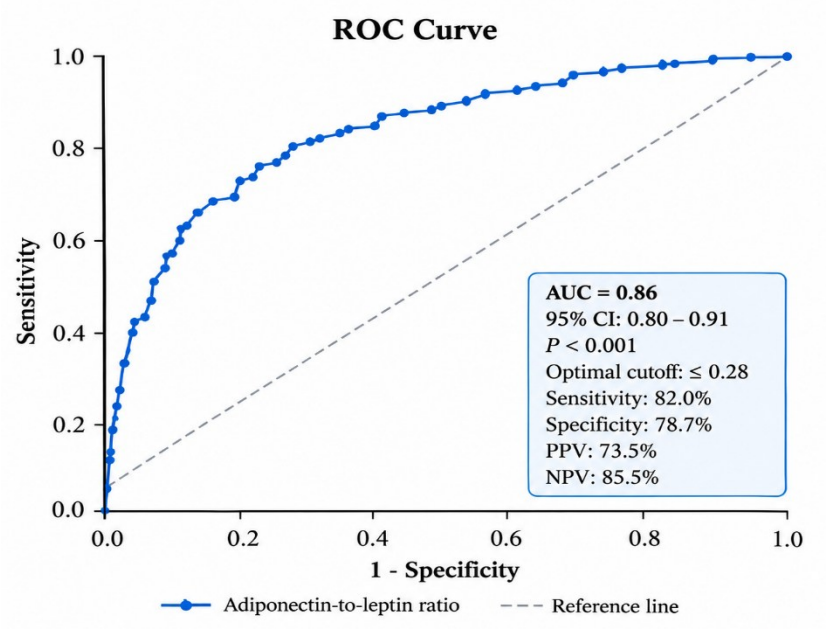

Figure 3. Receiver operating characteristic curve demonstrating the predictive performance of the adiponectin-to-leptin ratio for insulin resistance.

Predictive Value of the Adiponectin-to-Leptin Ratio for High Cardiometabolic Risk

The ALR was also shown to have high predictive power of high cardiometabolic risk (3 or more adverse cardiometabolic components). The ROC analysis showed an AUC of 0.82 (95% CI: 0.75–0.88; P < 0.001). The sensitivity and specificity of an ALR cutoff of ≤0.25 was 79.3% and 75.0%, respectively. Those whose ALR was < this threshold was much more likely to have more than one CMA (Fig. 4).

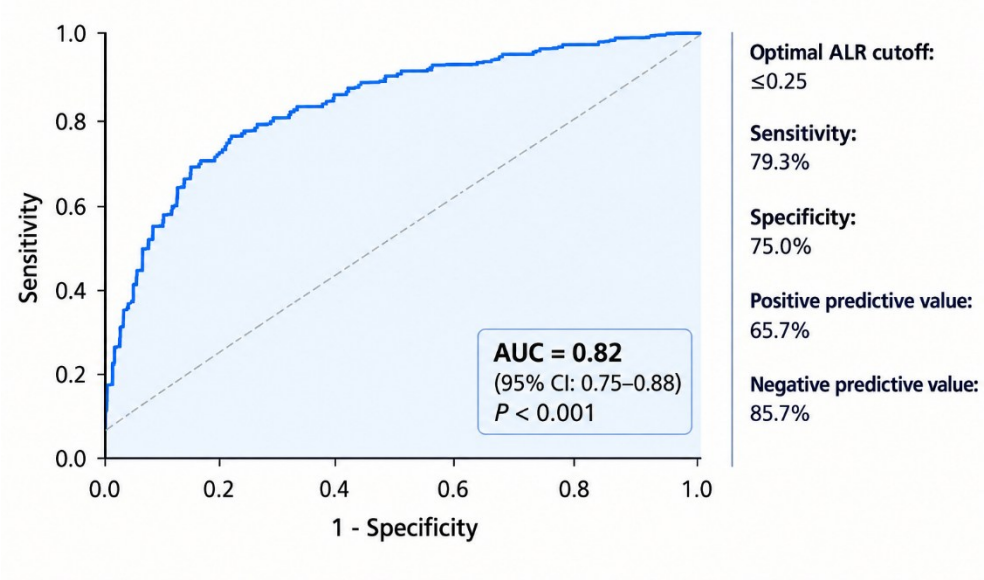

Figure 4. Receiver operating characteristic curve demonstrating the predictive performance of the adiponectin-to-leptin ratio for high cardiometabolic risk.

Comparison of Predictive Biomarkers

ALR was compared to adiponectin, leptin, BMI-for-age Z-score and HOMA-IR for discriminatory performance. For insulin resistance, ALR had a better discriminatory ability than either adiponectin or leptin alone. As predicted, HOMA-IR showed the highest discrimination as it was directly linked to the definition of insulin resistance, while ALR was an independent marker of metabolic risk based on the adipokines. Table 10 shows the comparative AUC values.

Table 10. Comparative ROC Performance of Selected Metabolic and Adipokine Parameters for Insulin Resistance

Predictor	AUC	95% CI	P-value
Adiponectin	0.74	0.66–0.81	<0.001
Leptin	0.79	0.72–0.85	<0.001
Adiponectin/leptin ratio	**0.86**	**0.80–0.91**	**<0.001**
BMI-for-age Z-score	0.78	0.71–0.84	<0.001
Waist-to-height ratio	0.81	0.74–0.87	<0.001

Multivariable Predictors of High Cardiometabolic Risk

To find independent predictors of high cardiometabolic risk, a second multivariable logistic regression model was developed. After controlling for age, sex, BMI-for-age Z score, and WC, the correlation between low ALR and high CMR remained significant for both men and females. After controlling for age, sex, BMI-for-age Z score, and WC in both men and females, the association between low ALR and high CMR remained strong. Participants with poor ALR had greater probabilities for three or more CMRCs (about 3.8 times higher). Additionally, waist circumference and BMI-for-age Z score had little bearing on the correlation between elevated cardiometabolic risk (Table 11).

Table 11. Multivariable Logistic Regression Analysis of Predictors of High Cardiometabolic Risk

Variable	Adjusted OR	95% CI	P-value
Age	1.05	0.88–1.26	0.592
Male sex	1.21	0.61–2.41	0.576
BMI-for-age Z-score	1.91	1.25–2.92	0.003
Waist circumference	1.05	1.02–1.08	<0.001
Triglycerides	1.01	1.00–1.02	0.044
Low adiponectin/leptin ratio	**3.82**	**1.89–7.73**	**<0.001**

Discussion

The obese group's much lower levels of adiponectin and higher levels of leptin are consistent with earlier research on youngsters. Adiponectin was shown to be negatively correlated with body weight and BMI in a study of obese children, whereas leptin was found to be greater than in non-obese children [11]. Similarly, Winer et al. demonstrated that obese children and adolescents had considerably lower levels of adiponectin, which is linked to a number of insulin resistance indices [12]. Adiponectin is a crucial marker for the investigation of adipocyte dysfunction as low levels have also been connected to elevated HOMA-IR, triglycerides, and other metabolic abnormalities in obese children [13].

When age, sex, BMI-for-age Z-score, waist circumference, and metabolic factors were included, the current research found a strong negative connection between ALR and HOMA-IR ($r = -0.61$, $P < 0.001$), and ALR was an independent predictor of HOMA-IR. This finding is in line with that of Frithioff-Bøjsøe et al., who examined more than 2,000 kids and teenagers and found that insulin resistance and cardiometabolic problems were associated with both leptin and adiponectin levels, but only the ratio of the two was strong enough to be examined independently [14]. In a similar vein, Vilela et al. discovered that children with and without MS differed considerably in the adiponectin/leptin ratio, HOMA-IR, and other metabolic parameters, highlighting the significance of the ratio as a marker of metabolic dysfunction [15].

Our study's findings also shown that when the number of cardiometabolic risk factors increased, ALR gradually decreased. The ALR was much lower in individuals with three or more risk factors than in those without severe metabolic abnormalities. This result is consistent with a large-scale research conducted in China on children and adolescents, which found that a rising leptin/adiponectin imbalance corresponded with more metabolic syndrome components and that the ratio outperformed either leptin or adiponectin alone [16]. The relationship between adipokine imbalance and early metabolic abnormalities of the cardiometabolic system is also shown in the IDEFICS trial, which found that children with high leptin levels and the leptin/adiponectin ratio had a greater risk of metabolic syndrome [17].

ALR is a possible comprehensive measure for cardiometabolic risk, as shown by its high negative connection with triglycerides, LDL-C, blood pressure, and hs-CRP and its positive correlation with HDL-C. In obese children, adiponectin has been shown to be positively correlated with HDL-C and negatively correlated with triglycerides, HOMA-IR, and inflammatory markers [18]. Additionally, irrespective of insulin resistance and obesity, low adiponectin levels have been linked to poorer lipid parameters and higher levels of CRP, indicating a possible connection between low adiponectin levels, inflammation, and metabolic syndrome [19].

Using ROC analysis, ALR's discriminating power in this research was fair for high cardiometabolic risk (AUC=0.82) and excellent for IR (AUC=0.86). Research of teenagers (ages 12 to 18) that showed the leptin/adiponectin ratio had a considerable diagnostic accuracy for insulin resistance and was more effective than either adiponectin or leptin alone supports the findings [20]. Strong correlations between the leptin/adiponectin ratio and many surrogate indicators for insulin resistance, including waist circumference, were recently found in a large study of prepubescent children [21].

The combination of both components' biological impacts may be responsible for ALR's comparatively high predictive power. While leptin levels are elevated in obesity and may be a marker of leptin resistance and adverse metabolic signals, adiponectin generally increases insulin sensitivity and has anti-inflammatory and cardioprotective qualities. Therefore, compared to any of the individual signals, the ratio could more accurately represent the imbalance between the potentially harmful and beneficial adipose-derived signals.

4. Conclusion

According to the present research, insulin resistance and increased cardiometabolic risk in obese children and adolescents are substantially correlated with decreased adiponectin to leptin ratios (ALR). After controlling for the primary confounding variables, reduced ALR was still linked to higher insulin resistance and high cardiometabolic risk. It was also strongly correlated with an elevated inflammatory state (HOMA-IR, hs-CRP), a worse lipid profile, central adiposity, hypertension, and a high cardiometabolic risk. Using ROC analysis with ALR, both insulin resistance and cardiometabolic risk were accurately predicted. These findings suggest that ALR may be utilized in conjunction with traditional anthropometric and biochemical criteria as an adipokine-based biomarker for the early diagnosis of childhood obesity with high metabolic risk. To validate the suggested cutoff values and assess their therapeutic efficacy, longitudinal research involving bigger and more varied pediatric populations are required.

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