

Multidimensional Analysis of Serum Adiponectin, Leptin, and Resistin Levels and Their Correlation with Childhood Obesity Based on Gut Microbiota and Inflammatory Markers: A Single-Center Cross-Sectional Retrospective Study

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Objective: To investigate the correlation between childhood obesity and gut microbiota diversity, inflammatory status, and serum adipokine levels through a single-center cross-sectional retrospective study.

Methods: This study was a single-center cross-sectional retrospective analysis. A total of 116 obese children were divided into three groups (A, B, and C) based on BMI overweight degree and 40 healthy children (group D) were also enrolled. The fecal samples and the gut microbiota alpha diversity index (Chao1, Observed species, PDwholetree) were analyzed through high-throughput sequencing of 16S rRNA. The fasting serum was collected and used to detect the levels of inflammatory markers (CRP, IL-1 β , TNF - α) and adipokines (adiponectin, leptin, resistin) by ELISA assay. The inter group comparison was conducted using analysis of variance, and the correlation was analyzed by Pearson analysis.

Results: Compared with the healthy control group, the diversity index of gut microbiota and adiponectin levels in the obese group were significantly reduced, and decreased with the severity of obesity. The levels of inflammatory markers, leptin, and resistin significantly increased, and increased with the severity of obesity (all $P < 0.05$). According to Pearson correlation analysis, Chao1 index, Observed specific index and PD whole tree index were positively correlated with serum adiponectin levels ($r = 0.584, 0.552, 0.415$, all $P < 0.001$), and negatively correlated with leptin ($r = -0.629, -0.614, -0.478$, all $P < 0.001$) and resistin ($r = -0.499, -0.444, -0.273$, $P < 0.01$). Serum CRP, IL-1 β , TNF - α were negatively correlated with adiponectin ($r = -0.565, -0.676, -0.709$, all $P < 0.001$), and positively correlated with leptin ($r = 0.509, 0.661, 0.749$, all $P < 0.001$) and resistin ($r = 0.457, 0.497, 0.533$, all $P < 0.001$).

Conclusion: This single-center study indicates that obese children exhibit reduced gut microbiota diversity, chronic low-grade inflammation, and lipid factor imbalance, and these three factors are interrelated, suggesting a potential synergistic effect in the development of childhood obesity.

Keywords: gut microbiota, inflammatory markers, adiponectin, leptin, resistin, childhood obesity

Introduction

With rising living standards and shifts in dietary patterns, the prevalence of obesity was increased markedly, establishing childhood obesity as a critical public health issue. The prevalence of overweight/obesity among children in developed countries exceeds 22%. In China, the rate was increased from 5.3% in 1995 to 20.5% in 2014, with a higher prevalence in males.¹ Studies have indicated that childhood obesity may lead to various non-communicable diseases and long-term health complications, such as hypertension² and coronary heart disease.³ Therefore, active diagnosis and intervention are essential to mitigate the impact of obesity on child development and long-term health outcomes.

Adipokines, key mediators linking adipose metabolism to systemic inflammatory responses, are thought to play a central role in obesity-related complications through their dysregulation.⁴ Serum adiponectin, leptin, and resistin are among the most studied adipokines. Adiponectin, an anti-inflammatory cytokine secreted by adipose tissue, enhances insulin sensitivity via activation of the AMPK signaling pathway.⁵ Although leptin is known for its role in energy metabolism, leptin receptor resistance under obese conditions leads to aberrant activation of the JAK-STAT pathway, contributing to chronic inflammation.⁶ Resistin is directly involved in the pathological regulation of the adipose–gut–immune axis, impairing intestinal barrier function through upregulation of pro-inflammatory cytokines such as IL-6 and TNF- α .⁷ Study has shown that serum levels of adiponectin, leptin, and resistin are significantly higher in obese children compared to those with normal weight, and are closely correlated with the activity of the renin–angiotensin–aldosterone system (RAS), suggesting their potential involvement in the pathogenesis of obesity.⁸

The association between gut microbiota and obesity has garnered growing research attention, although the precise mechanisms are not yet fully elucidated. Most existing studies have focused on “gut microbiota dysbiosis”—such as alterations in microbial composition—and its association with obesity,⁹ while dynamic changes in microbial diversity have received less attention. This is particularly relevant in children, in whom the interaction between gut microbiota development and adipokine regulation remains unclear. The gut microbiota of children is in the developmental stage and less stable than that of adults. They are more sensitive to interference such as diet and environment. A high-fat and high-sugar diet is more likely to rapidly change their microbiota structure, leading to a decrease in beneficial bacteria related to obesity and an increase in pathogenic bacteria.¹⁰ However, few studies have explored whether reduced microbial diversity contributes to obesity progression by influencing adipokine secretion and exacerbating inflammatory responses. Moreover, many studies have not integrated microbiota diversity, inflammatory markers, and adipokines within a unified analytical framework, limiting a comprehensive understanding of the molecular network underlying obesity. Therefore, this study aims to investigate the relationships among gut microbiota diversity, inflammatory markers, and serum levels of adiponectin, leptin, and resistin, in order to provide insights for future interventional strategies targeting gut microbiota modulation, inflammatory status, and adipokine levels in childhood obesity.

Materials and Methods

Baseline Data

The sample size was calculated using the G*Power 3.1 software: the primary outcome measure was the correlation between the intestinal microbiota Chao1 index and Adiponectin (effect size $r = 0.3$), with $\alpha = 0.05$ (two-tailed), $\beta = 0.2$ (80% confidence level). The calculated minimum sample size was 132 cases (100 cases in the obese group and 32 cases in the healthy group). This study actually included 156 cases (116 cases in the obese group and 40 cases in the healthy group). The sample size met the requirements of statistical testing and could effectively avoid Type II error. A retrospective analysis was conducted on the clinical data of 116 children with obesity who were diagnosed and treated in Beijing Shunyi Hospital between May 2022 and May 2025. The enrollment process was illustrated in Figure 1. Based on BMI value (exceeding the standard reference value by 20%–29%, 30%–49%, and $\geq 50\%$), the participants were categorized into three groups: mild BMI excess, moderate BMI excess, and severe BMI excess.¹¹

The mildly overweight children (Group A) included 58 participants (35 boys and 23 girls), aged 10–12 years, with a mean age of 11.21 ± 0.75 years; The moderately overweight group (Group B) consisted of 32 children (18 boys and 14 girls), aged 10–12 years, with a mean age of 11.15 ± 0.86 years; The severely overweight group (Group C) contained 26 children (15 boys and 11 girls), aged 10–12 years, with a mean age of 10.88 ± 0.80 years. Additionally, 40 children undergoing health examinations at our hospital during the same period were enrolled as healthy controls (Group D). These children had normal BMI values (ranging from 18.5 to 22.9 kg/m²) and a mean age of 11.12 ± 0.87 years (22 boys and 18 girls), aged 10–12 years. No significant differences in baseline characteristics were observed among the groups ($p > 0.05$).

Inclusion criteria: (1) meeting the diagnostic criteria for childhood obesity;¹² (2) no prior weight control interventions, including dietary management or medication; (3) well-developed organ systems; (4) sufficient cognitive ability to cooperate with research procedures. Exclusion criteria: (1) pathological obesity due to hormonal medications or other

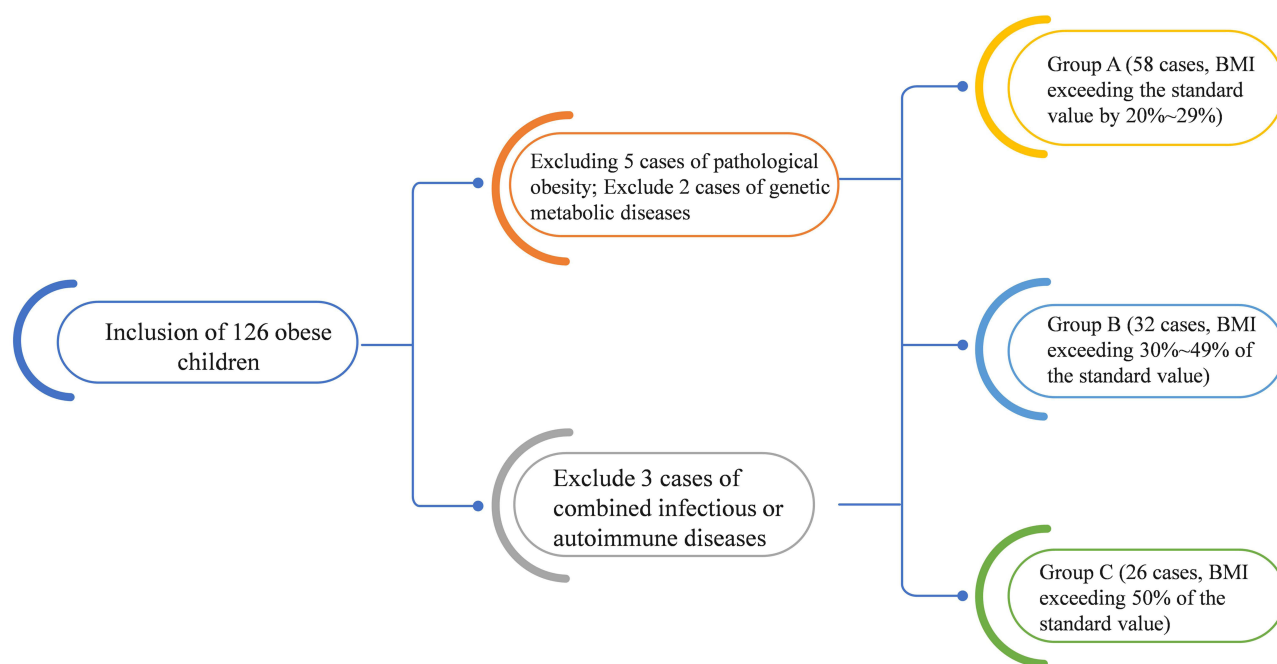


Figure 1 Flowchart of Patient Enrollment.

underlying causes; (2) history of antibiotic use within two weeks prior to the study; (3) presence of genetic or metabolic diseases; (4) comorbid infectious or autoimmune diseases.

Gut Microbiota Analysis

The gut microbiota composition and diversity were comprehensively profiled by sequencing the V3-V4 region of the 16S rRNA gene on the Illumina HiSeq high-throughput sequencing platform. The detailed procedures were as follows: Fresh fecal samples were collected from participants using sterile fecal collection devices containing DNA stabilizers. Immediately after collection, samples were placed in a -80°C pre-cooled dry ice shipping container and transferred to the central laboratory within 2 hours. Under a biosafety cabinet, each sample was aliquoted, and 150 mg was placed into a sterile cryovial for storage at -80°C until DNA extraction.

Genomic DNA was isolated from stool samples using the QIAamp Fast DNA Stool Mini Kit (Qiagen, Cat. No. 51604) according to the manufacturer's protocol. Key operation parameters: 1) Lysis step: After adding the lysis buffer, perform lysis at 95°C metal bath for 10 minutes; 2) Centrifugation parameters: After DNA binding, centrifuge at 8000 rpm for 1 minute to discard the waste liquid, and centrifuge at 14000 rpm for 2 minutes to collect the DNA during elution. The quality and quantity of the extracted DNA were evaluated with a NanoDrop 2000 spectrophotometer (Thermo Fisher) and a Qubit 3.0 Fluorometer (Thermo Fisher). Samples meeting the following criteria were used for downstream analyses: OD260/280 ratio between 1.7 and 1.9 (to exclude protein/organic contamination), OD260/230 ratio greater than 2.0 (to exclude polysaccharide/salt interference), and concentration ≥ 20 ng/ μL .

Targeted amplification was performed using universal primers for the V3-V4 region (341F: 5'-CCT AYG GGR BGC ASC AG-3'; 806R: 5'-GGA CTA CNN GGG TAT CTA AT-3', Synthetic Company: Sangon Biotech). The KAPA HiFi HotStart ReadyMix added to the PCR reaction system is a pre-mixed amplification reagent, whose core functions include providing high-fidelity DNA polymerase (reducing base mismatch rate), dNTPs (amplification raw materials), and optimizing the buffer (maintaining the stability of the reaction system). At the same time, HotStart technology was used to inhibit non-specific primer binding under low-temperature conditions, reducing the generation of non-target amplification products and ensuring the accuracy and specificity of the amplification sequencing results. The composition of the reaction mixture (25 μL) was: 2 $\times$ KAPA HiFi HotStart ReadyMix (12.5 μL , KAPA Biosystems, Cat No.: KK2602), upstream primer (0.2 μM), downstream primer (0.2 μM), template DNA (10 ng), and enzyme-free pure water

(supplemented to 25 μ L). Amplification products were confirmed by electrophoresis on a 1.5% agarose gel and subsequently purified using the AxyPrep DNA Gel Extraction Kit (Axygen). The purified amplicons were sequenced on the Illumina HiSeq 2500 platform using a paired-end 250 bp (PE250) strategy.

Raw sequencing reads were processed for quality control using Trimmomatic v0.39. This step is crucial, and it can remove low-quality bases (Q value < 20), adapter sequences, and chimeric reads, avoiding interference from poor quality sequences that may affect the accurate generation of Amplicon Sequence Variants (ASVs), and reducing false positive results in subsequent species annotation, thereby providing a reliable data basis for microbial diversity analysis. ASVs were inferred using the DADA2 pipeline, which includes built-in error rate estimation and correction. Instead of traditional OTUs (operational taxonomic units), DADA2 can improve the accuracy of microbiota composition analysis. In the taxonomic classification, species annotation was carried out using the SILVA138 reference database, which contains comprehensive 16SrRNA gene sequence information of prokaryotes, enabling classification and assignment of ASVs at the phylum, class, order, family, genus, and species levels.

Microbiota composition was analyzed at the phylum and genus levels to compare relative abundances and identify dominant species. Alpha diversity (within-sample diversity) was assessed using the following indices: the Chao1 index, the Observed-species index and the PD whole-tree index. All three indices were used to assess the Alpha diversity of the microbial communities within the samples, but they had different focuses in terms of function. The Chao1 index was used to estimate the potential total number of species in the community based on the distribution of species abundance, especially having a stronger ability to estimate low-abundance species (species that are easily overlooked), and may reflect the potential species richness of the community. The Observed-species index was used to directly count the actual number of observed species in the sample (in units of ASVs), intuitively reflecting the species richness already detected in the community, and the results were closer to the actual sequencing data. The function of the PDwholetree index was to calculate the total evolutionary distance between all species within the community based on the phylogenetic tree. It not only reflected the number of species, but also the genetic diversity and evolutionary differences between species, and evaluated the phylogenetic richness of the community. Compared with the Chao1 and Observed-species indices, the core difference of the PDwholetree index was that the former two only focus on the number of species (richness), without involving the phylogenetic relationship between species. While the PDwholetree index integrated the evolutionary information of species, it may distinguish communities with “the same number of species but significant differences in genetic background”, and more comprehensively reflects the biological significance of microbiota diversity. In addition, there were also Simpson index and Shannon index. The Simpson index quantified the dominance of species within a community, where values approaching 1 suggest reduced dominance and enhanced diversity. In contrast, the Shannon index incorporated both species richness and evenness, with elevated values indicating higher community diversity.

Each subject only had one fecal sample collection when they were included in the study. The sampling time window was set as the fasting state in the morning (with an 8–12 hour fasting period). The fecal samples were processed in the laboratory within 2 hours after collection to ensure the quality of the samples and the stability of the detection indicators.

Measurement of Serum Biomarkers

Fasting venous blood samples (4 mL) were obtained from all participants in the morning. The samples were centrifuged, and the supernatant was aliquoted for subsequent analysis. Levels of inflammatory cytokines, including C-reactive protein (CRP) (Cat No.: IC-CRP-p, Shanghai Yubo Biotechnology Co. Ltd., Lot No.: 20220415), interleukin-1 β (IL-1 β) (Cat No.: YBEA563Hu, Shanghai Yubo Biotechnology Co. Ltd., Lot No.: 20220508), and tumor necrosis factor- α (TNF- α) (Cat No.: YB-E10110, Shanghai Yubo Biotechnology Co., Ltd., Lot No.: 20220420), as well as serum adiponectin (Cat No.: NDC-KBB-ITVHNT-96, AmyJet Technology Co., Ltd., Lot No.: AM20220612), leptin (Cat No.: BEK-2057-2P, AmyJet Technology Co., Ltd., Lot No.: AM20220530), and resistin (Cat No.: BEK-2115-2P, AmyJet Technology Co., Ltd., Lot No.: AM20220605), were measured using enzyme-linked immunosorbent assays (ELISA) with a KD-810C fully automated microplate reader (Guangzhou Saibaichun Biotechnology Co., Ltd).

Each subject only had one serum sample collection during the time of inclusion in the study. The sampling time window was set as the fasting state in the morning (with an 8–12 hour fasting period). The serum sample was centrifuged

(at 3000 rpm for 10 minutes) and frozen at -80°C within 4 hours after collection to ensure the quality of the sample and the stability of the detection indicators.

Statistical Analysis

All statistical analyses were conducted using SPSS software (version 25.0). Categorical variables are summarized as number (percentage) and compared using the chi-square (χ^2) test. Firstly, the Shapiro–Wilk test combined with Q-Q plot was used to verify the normal distribution characteristics of the quantitative data: those that conform to the normal distribution were represented by mean $\pm$ standard deviation, a one-way ANOVA was used for multiple groups; the LSD test was employed for further pairwise comparisons. For non-normal distribution measurement data, they were represented by the median (quartiles) [M (Q1, Q3)], and the Mann–Whitney *U*-test or Kruskal–Wallis *H*-test was used for group comparisons. For indicators conforming to the normal distribution, Pearson correlation coefficient was used. Spearman correlation coefficient was used for skewed distribution indicators or ordinal classification indicators. For multivariate correlation analysis (such as the association between multiple microbiome indices and multiple adipokines), Bonferroni method was used for multiple test correction, and $P < 0.05$ after correction was considered statistically significant.

Results

Analysis of Gut Microbiota Diversity in Children with Different Degrees of Obesity

The moderate and severe overweight groups demonstrated significantly lower alpha diversity, as reflected by the Chao1, Observed-species, and PD whole tree indices, compared to the mild overweight group ($p < 0.05$; Table 1). Furthermore, the severe overweight group exhibited even lower values than the moderate overweight group ($p < 0.05$; Table 1). Relative to the healthy controls, all three overweight groups showed marked reductions in these diversity indices ($p < 0.05$; Table 1), with the mild overweight group maintaining higher values than both the moderate and severe overweight groups ($p < 0.05$; Table 1). In contrast, no significant differences were detected among the four groups for the Simpson and Shannon indices ($p < 0.05$; Table 1).

Comparison of Inflammatory Marker Levels Among Children with Different Degrees of Obesity

Concentrations of CRP, IL-1 β , and TNF- α were significantly elevated in the moderate and severe overweight groups relative to the mild overweight group ($p < 0.05$; Table 2), with the severe overweight group displaying higher levels than the moderate group ($p < 0.05$; Table 2). All overweight groups had significantly increased levels of these inflammatory markers compared to the healthy controls ($p < 0.05$; Table 2). Additionally, the mild overweight group showed lower inflammatory marker levels than both the moderate and severe overweight groups ($p < 0.05$; Table 2). These results indicate a graded elevation in proinflammatory cytokine levels corresponding to the severity of obesity.

Table 1 Analysis of Gut Microbiota Diversity in Children with Different Obesity Levels

Indicators	Mildly Overweight Group (n=58)	Moderately Overweight Group (n=32)	Severe Overweight Group (n=26)	Healthy Control Group (n=40)	F	p
Chao1 index	783.25 $\pm$ 76.75 ^a	715.66 $\pm$ 60.80 ^{ab}	623.79 $\pm$ 78.29 ^{abc}	832.41 $\pm$ 147.60	27.30	< 0.001
Observed-species index	501.30 $\pm$ 48.39 ^a	462.58 $\pm$ 72.53 ^{ab}	376.14 $\pm$ 57.04 ^{abc}	573.74 $\pm$ 61.85	62.37	< 0.001
Simpson index	0.90 $\pm$ 0.20 ^a	0.89 $\pm$ 0.27 ^{ab}	0.88 $\pm$ 0.28 ^{abc}	0.94 $\pm$ 0.23	0.44	0.727
Shannon index	4.80 $\pm$ 1.37 ^a	4.62 $\pm$ 1.34 ^{ab}	4.48 $\pm$ 1.26 ^{abc}	5.32 $\pm$ 1.55	2.43	0.067
PD whole tree index	23.41 $\pm$ 2.38 ^a	21.54 $\pm$ 1.14 ^{ab}	20.20 $\pm$ 1.96 ^{abc}	28.42 $\pm$ 2.76	91.31	< 0.001

Notes: Compared with the healthy control group, ^a $p < 0.05$; compared with the mildly overweight group, ^b $p < 0.05$; compared with the moderate overweight group, ^c $p < 0.05$.

Table 2 Comparison of Inflammatory Marker Levels Among Children with Different Obesity Levels

Inflammatory Factors	Mildly Overweight Group (n=58)	Moderately Overweight Group (n=32)	Severe Overweight Group (n=26)	Healthy Control Group (n=40)	F	P
CRP (mg/mL)	5.24±1.41 ^a	6.73±1.76 ^{ab}	8.11±1.98 ^{abc}	4.57±1.27	33.48	<0.001
IL-1 β (ng/mL)	1.94±0.51 ^a	3.13±0.80 ^{ab}	4.27±1.12 ^{abc}	1.55±0.34	106.55	<0.001
TNF- α (ng/mL)	1.16±0.32 ^a	1.94±0.45 ^{ab}	2.37±0.50 ^{abc}	0.89±0.27	112.55	<0.001

Notes: Compared with the healthy control group, ^a $p < 0.05$; compared with the mildly overweight group, ^b $p < 0.05$; compared with the moderate overweight group, ^c $p < 0.05$.

Table 3 Comparison of Serum Adiponectin, Leptin, and Resistin Levels in Children with Different Obesity Levels

Indicators	Mildly Overweight Group (n=58)	Moderately Overweight Group (n=32)	Severe Overweight Group (n=26)	Healthy Control Group (n=40)	F	P
Adiponectin (pg/L)	54.80±8.33 ^a	33.47±6.84 ^{ab}	17.71±2.46 ^{abc}	61.75±5.49	521.93	<0.001
Leptin (μ g/L)	10.24±1.35 ^a	17.16±4.19 ^{ab}	21.39±3.84 ^{abc}	8.42±1.72	163.99	<0.001
Resistin (μ g/L)	24.77±3.52 ^a	29.85±4.74 ^{ab}	35.36±4.49 ^{abc}	20.42±4.32	77.93	<0.001

Notes: Compared with the healthy control group, ^a $p < 0.05$; compared with the mildly overweight group, ^b $p < 0.05$; compared with the moderate overweight group, ^c $p < 0.05$.

Comparison of Serum Adiponectin, Leptin, and Resistin Levels Among Children with Different Degrees of Obesity

Compared with the mild overweight group, the moderate and severe overweight groups had significantly lower Adiponectin levels ($p < 0.05$, Table 3 and Figure 2), and the severe overweight group showed lower levels than the moderate group ($p < 0.05$, Table 3 and Figure 2). Relative to the healthy controls, all three overweight groups exhibited significantly reduced Adiponectin levels ($p < 0.05$, Table 3 and Figure 2), with the mild overweight group having higher levels than the moderate and severe groups ($p < 0.05$, Table 3 and Figure 2).

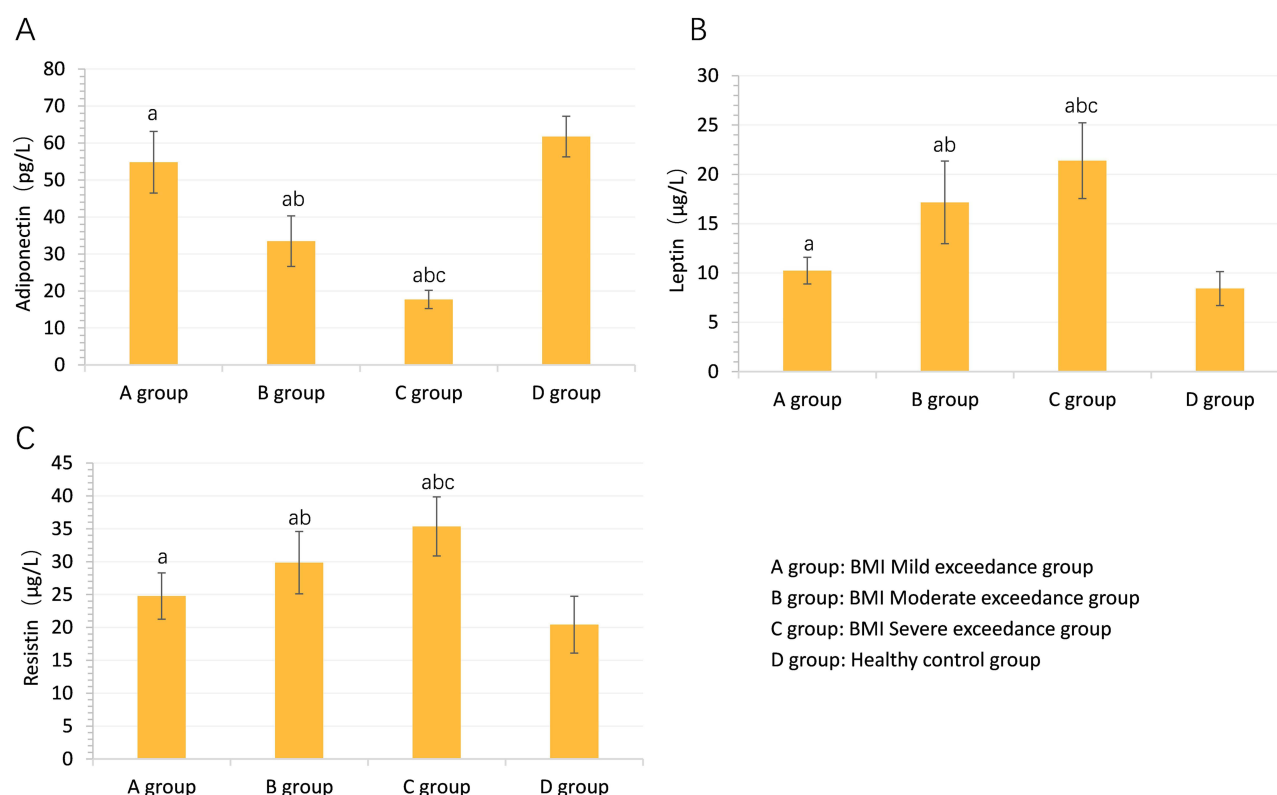


Figure 2 Comparison of Serum Adiponectin, Leptin, and Resistin Levels Among Children with Different Degrees of Obesity. (A) Adiponectin levels. (B) Leptin levels. (C) Resistin levels. Compared with the healthy control group (D group), ^a $p < 0.05$; compared with the mildly overweight group (A group), ^b $p < 0.05$; compared with the moderate overweight group (B group), ^c $p < 0.05$.

Table 4 Correlation Analysis Between Adipokines and Gut Microbiota

Indicators	Adiponectin		Leptin		Resistin	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Chao1 index	0.584		−0.629		−0.499	
Observed-species	0.552		−0.614		−0.444	
PD whole tree	0.415		−0.478		−0.273	0.003

Levels of both leptin and resistin were significantly elevated in the moderate and severe overweight groups relative to the mild overweight group ($p < 0.05$), with further increases observed in the severe compared to the moderate group ($p < 0.05$; Table 3 and Figure 2). Additionally, all three overweight groups exhibited markedly higher levels of these biomarkers compared to the healthy controls ($p < 0.05$). Within the overweight cohort, the mild group demonstrated lower concentrations than both the moderate and severe groups ($p < 0.05$; Table 3 and Figure 2). These results indicated that Adiponectin levels decreased progressively, while Leptin and Resistin levels increased gradually, with the aggravation of obesity. See Table 3 and Figure 2.

Correlation Between Adipokines and Gut Microbiota

Pearson correlation analysis demonstrated significant positive associations between serum adiponectin levels and alpha-diversity indices, including the Chao1, Observed species, and PD whole tree metrics ($p < 0.05$). Conversely, leptin and resistin levels exhibited markedly negative correlations with these microbial diversity indices (Table 4 and Figure 3).

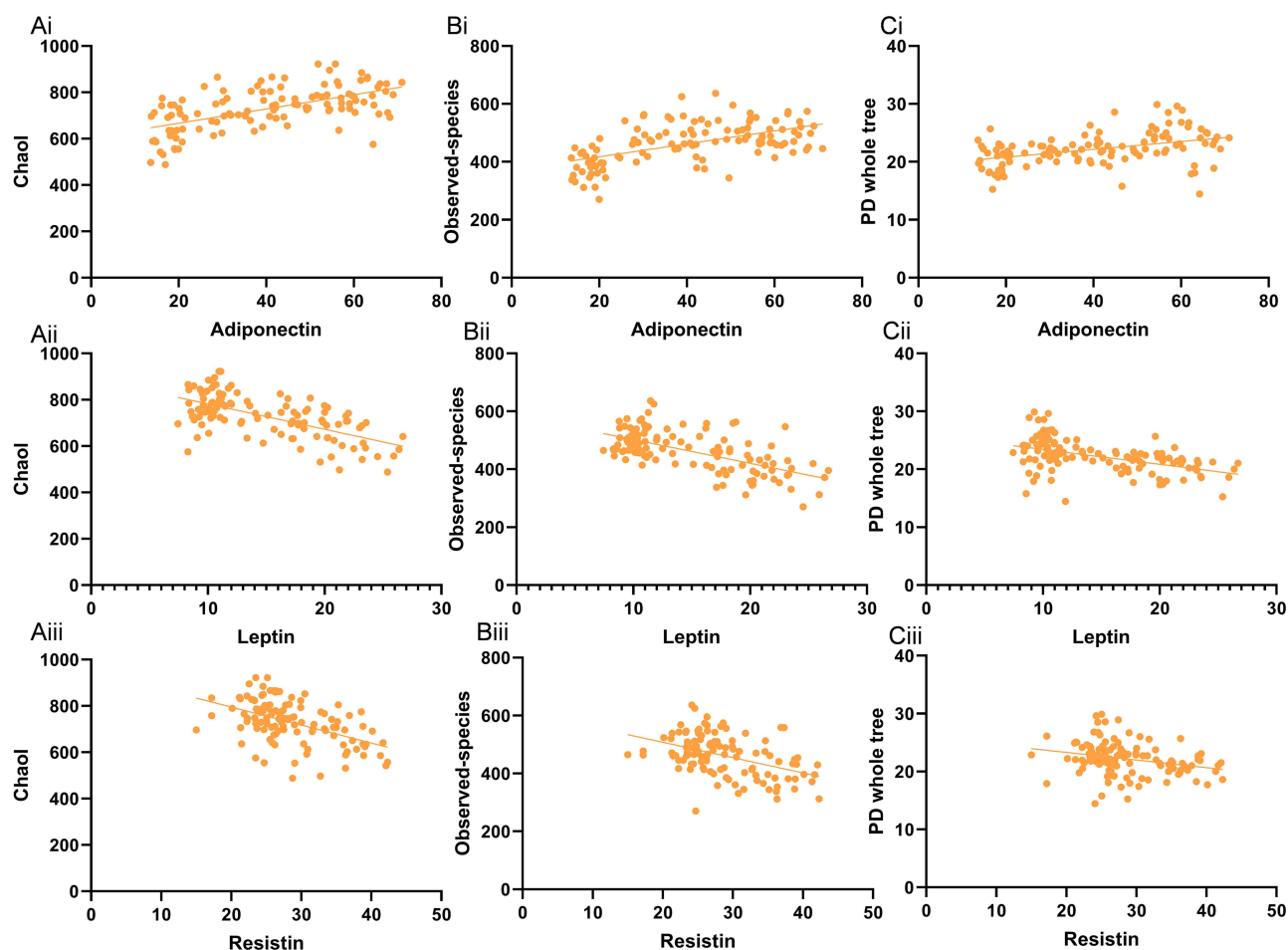


Figure 3 Correlation Analysis Between Gut Microbiota Diversity and Adipokine Levels. (Ai–Ci) The X-axis represents Adiponectin, while the Y-axis represents Chao1, Observed species, and PD whole tree, respectively. The scatter plots and fitted curves indicate a positive correlation between adiponectin levels and gut microbiota diversity. (Aii–Cii) The X-axis represents Leptin, and the Y-axis corresponds to the same indices as in (Ai–Ci), demonstrating a negative correlation between leptin levels and gut microbiota diversity. (Aiii–Ciii) The X-axis represents Resistin, and the Y-axis corresponds to the same indices as in (Ai–Ci), reflecting a negative correlation between resistin levels and gut microbiota diversity.

Table 5 Correlation Analysis Between Adipokines and Inflammatory Factors

Indicators	Adiponectin		Leptin		Resistin	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
CRP	−0.565		0.509		0.457	
IL-1 β	−0.676		0.661		0.497	
TNF- α	−0.709		0.749		0.533	

Correlation Analysis Between Adipokines and Inflammatory Factors

Significant negative correlations were observed between serum adiponectin concentrations and levels of the inflammatory markers CRP, IL-1 β , and TNF- α ($p < 0.05$; Table 5 and Figure 4). In contrast, leptin and resistin showed significant positive correlations with these proinflammatory cytokines ($p < 0.05$; Table 5 and Figure 4).

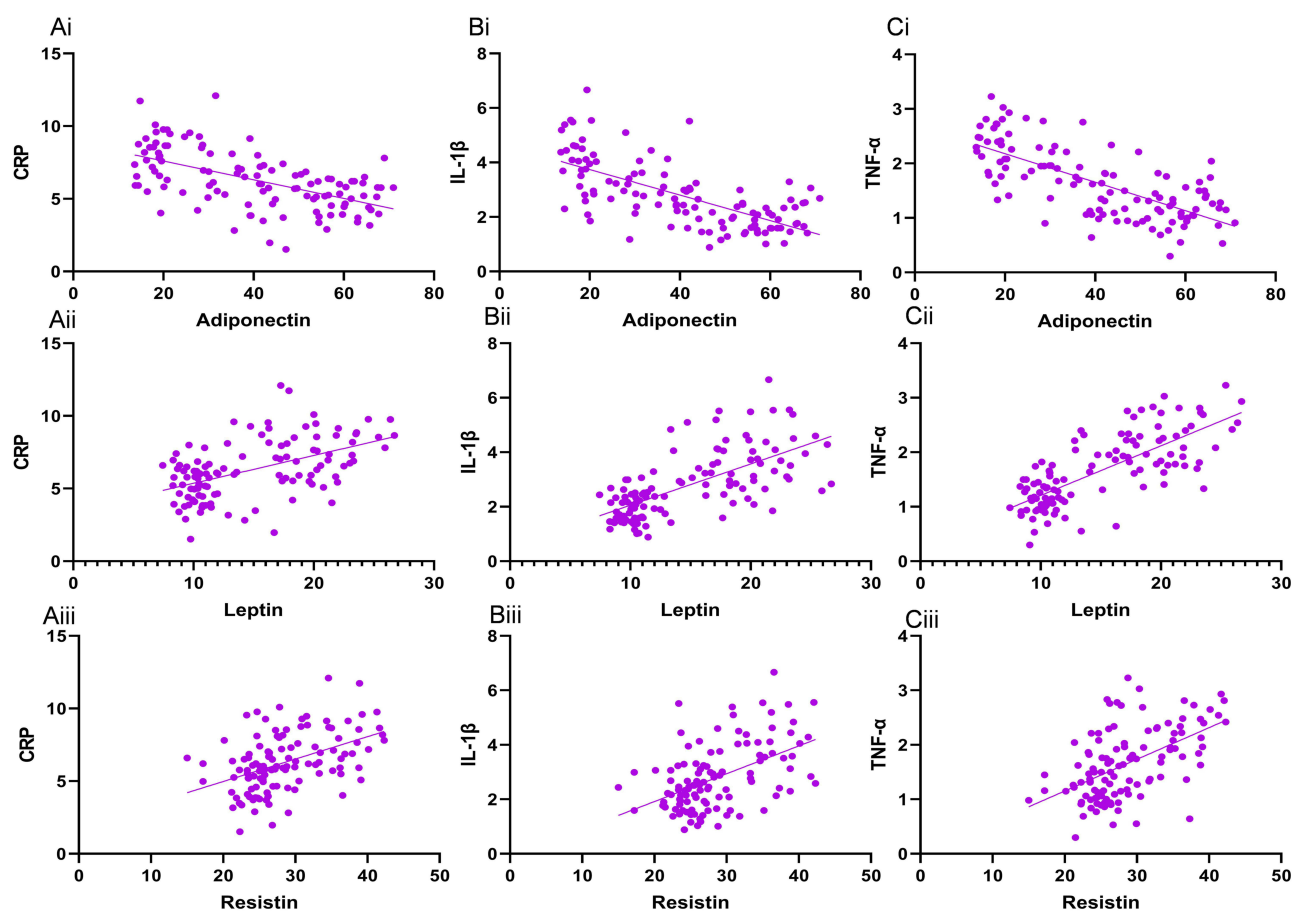


Figure 4 Correlation Analysis Between Inflammatory Cytokines and Adipokine Levels. **(Ai–Ci)** The X-axis represents Adiponectin, while the Y-axis represents CRP, IL-1 β , and TNF- α , respectively. The results show a negative correlation between adiponectin and inflammatory cytokine levels. **(Aii–Cii)** The X-axis represents Leptin, and the Y-axis corresponds to the same inflammatory markers as in **(Ai–Ci)**, indicating a positive correlation between leptin and inflammatory cytokine levels. **(Aiii–Ciii)** The X-axis represents Resistin, and the Y-axis corresponds to the same indices as in **(Ai–Ci)**, reflecting a positive correlation between resistin levels and inflammatory cytokine levels.

Discussion

Childhood obesity is a multifactorial condition influenced by diet, genetics, and lifestyle. Additionally, gut microbiota and their metabolites play a crucial role in the progression of childhood obesity by regulating neurological and immune system development, as well as intestinal barrier function.¹³ Under physiological conditions, the gut microbiota maintains a dynamic equilibrium. Disruption of this balance alters microbial composition, contributing to obesity and other metabolic disorders.¹⁴ Studies have shown that children's gut microbiota responds more intensely to obesity-related factors than that of adults, indicating a greater susceptibility to dysbiosis in obese children.¹⁴ Animal studies have demonstrated that fecal microbiota transplantation (FMT) can alter body phenotypes: mice receiving transplants from obese donors developed obesity, whereas those receiving transplants from healthy donors maintained a normal weight. This suggests that restoring a healthy gut microbiota may reverse dysbiosis, potentially through repairing intestinal barrier damage and alleviating metabolic inflammation.¹⁵ Thus, gut dysbiosis is closely associated with the development and progression of childhood obesity, and modulating the gut microbiota may represent a promising intervention strategy.

Gut microbiota diversity is a core indicator of microbial ecological balance. The Chao1 index estimates potential species richness, reflecting the total number of species likely present in the community, while the Observed-species index quantifies the actual number of species detected. Together, these indices reflect the "species richness" of the gut microbiota.¹⁶ The PD whole tree index evaluates phylogenetic diversity based on evolutionary distances between species, representing the breadth of genetic divergence within the community.¹⁴ In this study, we observed a gradual decrease in the Chao1, Observed-species, and PD whole tree indices with increasing severity of obesity, indicating that there is a correlation between the diversity of gut microbiota and the degree of obesity. Reduced microbial diversity may lead to an increase in conditional pathogens, disrupt gut ecological balance, impair normal metabolism, and ultimately contribute to obesity. However, there may be overlap in the distribution of data between groups. Although the mean difference is statistically significant, the actual biological difference still requires further verification.

Using Pearson correlation analysis, this study identified significant associations between adipokines and gut microbiota diversity: the Chao1, Observed-species, and PD whole tree indices were positively correlated with serum adiponectin levels and negatively correlated with leptin and resistin levels. There is a statistical correlation between gut microbiota diversity and levels of adipokines, but the independent clinical significance of them remains unclear due to the lack of control for potential confounding factors such as age and gender. A diverse microbiota may help maintain metabolic homeostasis by promoting adiponectin synthesis and secretion while suppressing excessive leptin and resistin expression. Conversely, reduced microbial diversity may impair adipokine regulation, leading to decreased adiponectin and elevated leptin and resistin levels, thereby exacerbating energy metabolism imbalance and inflammatory responses. This creates a vicious cycle of "dysbiosis-adipokine imbalance-obesity progression." The positive correlation between adiponectin and microbial diversity may be attributed to certain probiotics (eg, *Bifidobacterium*, *Akkermansia*) and their metabolites (eg, short-chain fatty acids), which stimulate adiponectin secretion. In turn, adiponectin may help maintain microbial stability by enhancing intestinal barrier function.¹⁷ On the other hand, elevated leptin and resistin levels may be linked to endotoxemia resulting from abnormal microbiota structure. Endotoxins activate inflammatory pathways such as TLR4, which induce leptin resistance and resistin overexpression, further damaging microbial diversity.¹⁸ The above correlation suggests that the decrease in gut microbiota diversity may exacerbate metabolic disorders and adipokines imbalances through specific mechanisms. Firstly, a decrease in diversity is often accompanied by a reduction in short-chain fatty acid (SCFA)-producing bacteria such as *Bifidobacterium* and *Akkermansia*. Insufficient SCFAs (such as butyric acid) can weaken the intestinal barrier function, leading to the translocation of endotoxins (LPS) into the bloodstream, activating the Toll like receptor 4 (TLR4) - mediated inflammatory pathway, thereby inducing leptin resistance and upregulating resistin expression.¹⁹ Meanwhile, SCFAs themselves are also key signaling molecules that regulate the energy metabolism and satiety of host, and their reduction directly promotes fat storage and insulin resistance.²⁰ Secondly, the metabolites or cellular components of specific beneficial bacteria (such as *Bifidobacterium* and *Akkermansia*) can promote the secretion of adiponectin in adipose tissue by activating pathways such as peroxisome proliferator-activated receptor gamma (PPAR- γ), thereby improving insulin sensitivity.²¹ Therefore, increasing diversity can increase the abundance of beneficial bacteria (such as short-chain fatty acid producing bacteria) and reduce endotoxin

production, thereby promoting adiponectin secretion, inhibiting abnormal expression of leptin and resistin, and improving chronic low-grade inflammation, which can be a potential treatment strategy for obesity.

Previous studies have confirmed that levels of inflammatory factors such as TNF receptor-associated factor 6 (TRAF6) and chemokine CXCL2 are higher in obese children than in normal-weight children and are positively correlated with BMI.²² This study found that serum levels of CRP, IL-1 β , and TNF- α gradually increased with the degree of obesity. This may be due to a low-grade, persistent inflammatory response triggered by metabolic cells in reaction to nutrient and energy surplus, which further disrupts endocrine and paracrine signaling and normal metabolism.²³ Adipose tissue is considered a central organ in obesity-related inflammation. During sustained energy surplus, adipocytes undergo hyperplasia and hypertrophy to store excess energy, leading to increased adiposity and BMI. When mechanical and metabolic stress exceeds a certain threshold, intracellular signals may activate inflammatory pathways.²⁴ Adiponectin, leptin, and resistin are adipokines that may synergistically or antagonistically regulate metabolism and influence the progression of low-grade inflammatory diseases.^{25,26} Adiponectin, an anti-inflammatory hormone secreted by adipocytes, is closely associated with insulin sensitivity and lipid oxidation. Obese children show decreased adiponectin and increased leptin levels, which are correlated with metabolic disorders.²⁷ Leptin, the product of the obesity gene, binds to and activates leptin receptors, playing a key role in body weight regulation. Obesity is often associated with leptin resistance, leading to hyperleptinemia and elevated resistin, which promote the expression of inflammatory factors such as IL-1 β and TNF- α , thereby exacerbating tissue damage.²⁸ Adiponectin suppresses inflammation through the AMPK signaling pathway, and its deficiency may worsen metabolic abnormalities in obesity.²⁹ Leptin resistance abnormally activates the JAK-STAT pathway, inducing release of IL-1 β and TNF- α , while resistin upregulates pro-inflammatory factors and disrupts the intestinal barrier, forming a pathological “adipose-gut-immune” axis.³⁰ The concept of this axis emphasizes the dynamic interaction between adipose tissue, gut microbiota, and the immune system: adipokines secreted by adipose tissue can affect gut permeability and microbiota composition. The gut microbiota and its metabolites can regulate systemic low-grade inflammatory state and the expression of adipokines. The sustained immune inflammatory response, in turn, negatively affects fat metabolism and intestinal environment, forming a mutually amplifying closed loop that plays a central role in the occurrence and development of obesity and its complications.³¹ This study identified significant correlations between inflammatory markers (CRP, IL-1 β , TNF- α) and adipokines: all three were negatively correlated with adiponectin and positively correlated with leptin and resistin. This indicates that chronic inflammation in obesity may bidirectionally regulate adipokine balance. And current research supports the existence of a bidirectional promoting relationship between the two. On the one hand, an imbalance of adipokines can drive inflammation: the level of adiponectin decreases, and its anti-inflammatory effect is weakened by inhibiting NF- κ B activation through the AMPK pathway.³² Leptin resistance and high levels of leptin can abnormally activate the JAK2/STAT3 pathway in macrophages and adipose tissue, promoting the production of inflammatory factors such as IL-6 and TNF- α . Resistin can directly stimulate monocytes to produce TNF- α , IL-6, etc., and disrupt the intestinal barrier, promoting the entry of endotoxins into the bloodstream.³³ On the other hand, chronic low-grade inflammation can exacerbate the disorder of adipokines, and inflammatory factors such as TNF- α and IL-1 β can inhibit the expression and secretion of adiponectin genes. The activation of inflammatory pathways can interfere with the downstream signal transduction of leptin receptors, and aggravate leptin resistance.³⁴ Dysregulation of adipokines exacerbates the bidirectional vicious cycle of inflammatory response, which may be an important mechanism for the sustained progression and difficult reversal of obesity.

The experimental methods for verifying the causal relationship between gut microbiota diversity and adipokine secretion include fecal microbiota transplantation (FMT) experiments, germ-free mouse colonization models, clinical trials of probiotic/prebiotic intervention, and longitudinal cohort dynamic monitoring of the changes in microbiota and adipokines. Inflammation promotes the vicious cycle of obesity through bidirectional regulation. Inflammatory factors inhibit the synthesis of Adiponectin and activate the secretion of Leptin/Resistin, exacerbating the imbalance in energy metabolism. And the imbalance of adipokines further damages the intestinal barrier, increases the entry of endotoxins into the bloodstream, induces more severe inflammatory response, and forms a continuously amplified pathological cycle.³⁵ In the future, a combined intervention strategies targeting the “gut microbiota-adipokines-inflammation” axis can be developed (such as the synergistic use of probiotics and anti-inflammatory agents), screening functional strains that can specifically regulate the balance of Adiponectin/Leptin, optimizing the formula of probiotic supplement, and provide new targets for precise treatment of obesity.

Limitations

This study was a single-center cross-sectional survey with a relatively single sample source, and its conclusions may be influenced by specific population and regional factors. In the future, we will conduct multi-center, prospective cohort studies that include samples from a wider range of regions and population characteristics to validate the generalizability of current findings and further explore the dynamic causal relationships between gut microbiota, adipokines, and inflammatory markers. Furthermore, this study only revealed the correlations between variables but did not establish causal relationships. It also did not provide experimental evidence that the regulation of gut microbiota or the inhibition of inflammation can improve obesity. Therefore, it cannot be directly inferred that the above factors can be used as intervention targets for childhood obesity. At the same time, this study did not quantify the explanatory power of Adiponectin, Leptin, Resistin, and gut microbiota diversity on BMI variation through methods such as multiple regression analysis. Also, it did not compare the relative weights of the roles of microbial and adipogenic factors in obesity related mechanisms. As a result, the importance hierarchy of each factor is still unclear, and the network mechanism among the three factors has not been further validated through mediation or pathway analysis. Although the results suggest that gut microbiota may affect inflammatory status through adipokine signaling, this hypothesis remains speculative due to the lack of support from multivariate pathway models and needs to be validated through more complex statistical methods or experimental designs in the future.

Conclusion

In conclusion, obese children exhibited gut microbiota dysbiosis and a low-grade inflammatory state, which were correlated with serum levels of adiponectin, leptin, and resistin. There is a significant correlation among these three factors, suggesting that they may be associated with the occurrence and development of childhood obesity. Regulating the diversity of gut microbiota can be a potential treatment strategy for obesity. The core reason is that increasing microbiota diversity can increase the abundance of beneficial bacteria, reduce endotoxin production, thereby promoting Adiponectin secretion, inhibiting abnormal expressions of Leptin and Resistin, improving the chronic low-grade inflammatory state, and breaking the imbalanced pathological cycle. Probiotic supplements optimize the microbiota structure by colonizing the intestine, and their metabolites can directly regulate the balance of adipokines, while inhibiting the release of pro-inflammatory factors (CRP, IL-1 β) and alleviating the interference of inflammation on metabolism.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by The Ethics Committee of Ankang Traditional Chinese Medicine Hospital (2025AKZYLL-KY011-03).

Consent to Participate

Written Informed consent was obtained from every human participant's parents or legal guardians in the study and all agree to publish the research results.

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Disclosure

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References

1. Zhang S, Dang Y. Roles of gut microbiota and metabolites in overweight and obesity of children. *Front Endocrinol.* **2022**;13:994930. doi:10.3389/fendo.2022.994930
2. Vasile CM, Padovani P, Rujinski SD, et al. The Increase in Childhood Obesity and Its Association with Hypertension during Pandemics. *J Clin Med.* **2023**;12(18):5909. doi:10.3390/jcm12185909
3. Liu L, Wu KCH, Cai A, Xu A, Y CBM. Childhood psychosocial adjustment and midlife obesity, diabetes and hypertension: prospective study from two birth cohorts. *Bri J Psychiat.* **2024**;225(6):563–571. doi:10.1192/bjp.2024.133
4. Tilg H, Ianiro G, Gasbarrini A, Adolph TE. Adipokines: masterminds of metabolic inflammation. *Nat Rev Immunol.* **2025**;25(4):250–265. doi:10.1038/s41577-024-01103-8
5. Scott SR, Millwood SN, Manczak EM. Adipocytokine correlates of childhood and adolescent mental health: a systematic review. *Developmental Psychobiol.* **2023**;65(3):e22379. doi:10.1002/dev.22379
6. Ismaiel A, Kiessling M-L, Ismaiel M, et al. The Role of Adipokines in Chronic Pancreatitis. A Systematic Review and Meta-Analysis. *JGLD.* **2024**;33(3):394–404. doi:10.15403/jgld-5739
7. Reddy A, P Della Gatta, S Mason, et al. Adherence to a Mediterranean diet may improve serum adiponectin in adults with nonalcoholic fatty liver disease: the MEDINA randomized controlled trial. *Nutr Res.* **2023**;119:98–108.
8. Kirk B, Mooney K, Vogrin S, et al. Leucine-enriched whey protein supplementation, resistance-based exercise, and cardiometabolic health in older adults: a randomized controlled trial. *J Cachexia Sarcopenia Muscle.* **2021**;12(6):2022–2033. doi:10.1002/jcsm.12805
9. Luo Y, Li M, Luo D, Tang B. Gut Microbiota: an Important Participant in Childhood Obesity. *Adv Nutr.* **2025**;16(2):100362. doi:10.1016/j.advnut.2024.100362
10. Lu M, Feng R, Li M, et al. Causal relationship between gut microbiota and childhood obesity: a Mendelian randomization study and case-control study. *Clin Nutr ESPEN.* **2024**;63:197–206. doi:10.1016/j.clnesp.2024.05.012
11. Tung JYL, Poon GWK, Du J, Wong KKY. Obesity in children and adolescents: overview of the diagnosis and management. *Chronic Dis Transl Med.* **2023**;9(2):122–133. doi:10.1002/cdt3.58
12. Taveras EM, Hohman KH, Price SN, et al. Correlates of participation in a pediatric primary care-based obesity prevention intervention. *Obesity.* **2011**;19(2):449–452. doi:10.1038/oby.2010.207
13. Epstein LH, Wilfley DE, Kilanowski C, et al. Family-Based Behavioral Treatment for Childhood Obesity Implemented in Pediatric Primary Care: a Randomized Clinical Trial. *JAMA.* **2023**;329(22):1947–1956. doi:10.1001/jama.2023.8061
14. Yu Z, Yu XF, Zhao X, Su Z, Ren PG. Greater alteration of gut microbiota occurs in childhood obesity than in adulthood obesity. *Front Pediatrics.* **2023**;11:1087401.
15. Zhu X, Zhao L, Lei L, et al. Fecal microbiota transplantation ameliorates abdominal obesity through inhibiting microbiota-mediated intestinal barrier damage and inflammation in mice. *Microbiol Res.* **2024**;282:127654.
16. Abomoelak B, Pemberton V, Deb C, et al. The Gut Microbiome Alterations in Pediatric Patients with Functional Abdominal Pain Disorders. *Microorganisms.* **2021**;9(11):2354. doi:10.3390/microorganisms9112354
17. Driuchina A, Isola V, Hulmi JJ, et al. Unveiling the impact of competition weight loss on gut microbiota: alterations in diversity, composition, and predicted metabolic functions. *J Int Soc Sports Nutr.* **2025**;22(1):2474561. doi:10.1080/15502783.2025.2474561
18. Zieba DA, Biernat W, Baré J. Roles of leptin and resistin in metabolism, reproduction, and leptin resistance. *Domestic Animal Endocrinol.* **2020**;73:106472.
19. Xu XL, Zhao Y, Chen MM, Wu SJ, Yu K, Lian ZX. Shifts in intestinal microbiota and improvement of sheep immune response to resist Salmonella infection using Toll-like receptor 4 (TLR4) overexpression. *Front Microbiol.* **2023**;14:1075164. doi:10.3389/fmicb.2023.1075164
20. Xiong L, Yao X, Pei J, et al. Do microbial-gut-muscle mediated by SCFAs, microbial-gut-brain axis mediated by insulin simultaneously regulate yak IMF deposition? *Int J Biol Macromol.* **2024**;257(Pt 1):128632. doi:10.1016/j.ijbiomac.2023.128632
21. Wu Z, Zuo X, Wang X, et al. The probiotic Lactobacillus casei Zhang-mediated correction of gut dysbiosis ameliorates peritoneal fibrosis by suppressing macrophage-related inflammation via the butyrate/PPAR- γ /NF- κ B pathway. *Food Funct.* **2023**;14(15):6840–6852. doi:10.1039/D3FO01518A
22. He E, Chang K, Dong L, et al. Identification and Validation of CXCL2 as a Key Gene for Childhood Obesity. *Biochem Genet.* **2024**;62(4):2743–2765. doi:10.1007/s10528-023-10566-8
23. Ramon-Krauel M, Leal-Witt MJ, Osorio-Conles Ó, et al. Relationship between adiponectin, TNF α , and SHBG in prepubertal children with obesity. *Molecular Cellular Pediat.* **2021**;8(1):3. doi:10.1186/s40348-021-00113-z
24. Lang H, Loudermilk EN, Clark WA, et al. Inflammatory markers and body mass index among hispanic children. *PLoS One.* **2024**;19(6):e0289523. doi:10.1371/journal.pone.0289523
25. Graff EC, Fang H, Wanders D, Judd RL. The Absence of Adiponectin Alters Niacin's Effects on Adipose Tissue Inflammation in Mice. *Nutrients.* **2020**;12(8):2427. doi:10.3390/nu12082427
26. Polak-Szczybyło E, Tabarkiewicz J. The Influence of Body Composition, Lifestyle, and Dietary Components on Adiponectin and Resistin Levels and AR Index in Obese Individuals. *Int J Mol Sci.* **2025**;26(1):393. doi:10.3390/ijms26010393
27. Xu X, Du Y, Wang N. Association Between Circulating Resistin Level and Preeclampsia: a Meta-Analysis. *Hormone Metab Res.* **2023**;55(12):835–845. doi:10.1055/a-2167-0179
28. Aisike G, Kuerbanjiang M, Muheyati D, et al. Correlation analysis of obesity phenotypes with leptin and adiponectin. *Sci Rep.* **2023**;13(1):17718. doi:10.1038/s41598-023-43550-8
29. Xu N, Zhang Y, Doycheva DM, et al. Adiponectin attenuates neuronal apoptosis induced by hypoxia-ischemia via the activation of AdipoR1/APPL1/LKB1/AMPK pathway in neonatal rats. *Neuropharmacology.* **2018**;133:415–428.
30. Lo KA, Huang S, Walet ACE, et al. Adipocyte Long-Noncoding RNA Transcriptome Analysis of Obese Mice Identified Lnc-Leptin, Which Regulates Leptin. *Diabetes.* **2018**;67(6):1045–1056. doi:10.2337/db17-0526
31. Morris A. Gut microbiota: link between the gut and adipose tissues. *Nat Rev Endocrinol.* **2017**;13(9):501.
32. Shao W, Wu J, Zhu M, Wang Y, Ci H. Effects of GLP-1 Receptor Agonist on Glycolipid Metabolism and Micro Inflammatory Status in Patients with Abdominal Obesity and Type 2 Diabetes. *Alternative Therap Health Med.* **2024**;2024:1.

33. Paixão de Gois B, Figueiredo N, Soares Lopes KL, et al. The impact of the obesity onset on the inflammatory and glycemic profile of women with severe obesity. *Surg Obesity Related Dis.* 2024;20(10):976–983. doi:10.1016/j.soard.2024.04.015
34. Bapat SP, Whitty C, Mowery CT, et al. Obesity alters pathology and treatment response in inflammatory disease. *Nature.* 2022;604(7905):337–342. doi:10.1038/s41586-022-04536-0
35. Huerta-Canseco C, Caba M, Camacho-Morales A. Obesity-mediated Lipoinflammation Modulates Food Reward Responses. *Neuroscience.* 2023;52:937–953.

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