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Article

Association Between Insulin Resistance and Serum 25-Hydroxyvitamin D, Insulin-Like Growth Factor-1, and Blood Lipid Profiles in Children With Obesity

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Abstract

Aims/Background: Obesity in children was associated with insulin resistance (IR) and is often accompanied by dyslipidemia. 25-hydroxyvitamin D (25-(OH)D) and insulin-like growth factor-1 (IGF-1) have been implicated in IR. The purpose of this study was to explore the correlation between IR and serum 25-(OH)D, IGF-1, and blood lipid profiles in children with obesity. **Methods:** A total of 125 children with obesity who attended The Affiliated Yangming Hospital of Ningbo University between January 2023 and April 2025 were retrospectively analyzed. According to insulin sensitivity, participants were divided into two groups: the insulin-sensitive group (n = 56, Homeostasis Model Assessment of Insulin Resistance [HOMA-IR] <3.16) and the insulin-resistant group (n = 69, HOMA-IR ≥3.16). Serum 25-(OH)D, IGF-1, and lipid profiles [triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)] were measured. Binary logistic regression analysis and receiver operating characteristic (ROC) analyses were performed to investigate the association between IR and these biomarkers. **Results:** Fasting insulin and HOMA-IR levels were significantly higher in the insulin-resistant group than in the insulin-sensitive group ($p < 0.001$). Compared with the insulin-sensitive group, levels of 25-(OH)D, IGF-1, and HDL-C were significantly lower in the insulin-resistant group ($p < 0.001$, $p = 0.032$, and $p = 0.023$, respectively), while TG and LDL-C levels were significantly higher ($p < 0.001$). No significant difference was observed in TC levels between the two groups ($p = 0.334$). Multivariate analysis identified 25-(OH)D (odds ratio [OR] = 0.934, 95% confidence interval [CI]: 0.877–0.995, $p = 0.035$), IGF-1 >238.68 (OR = 0.303, 95% CI: 0.103–0.894, $p = 0.031$), TG (OR = 3.979, 95% CI: 1.461–10.835, $p = 0.007$), and LDL-C (OR = 2.625, 95% CI: 1.398–4.928, $p = 0.003$) as independent factors associated with IR in children with obesity. ROC analysis showed that the areas under the curves (AUCs) for 25-(OH)D, IGF-1, TG, LDL-C, and the combined indicator were 0.692, 0.612, 0.775, 0.747, and 0.856, respectively ($p < 0.001$, $p = 0.025$, $p < 0.001$, $p < 0.001$, and $p < 0.001$). **Conclusion:** In children with obesity, serum 25-(OH)D, IGF-1, TG, and LDL-C are significantly associated with IR.

Keywords: 25-hydroxyvitamin D; insulin resistance; insulin-like growth factor-1; pediatric obesity

1. Introduction

Obesity has reached pandemic proportions worldwide, with the prevalence in both children and adults steadily increasing [1,2]. The rate of obesity in children remains high and has continued to rise in recent years, becoming a major global health concern [3]. A study predicted that by 2030, the prevalence of overweight and obesity will reach 31.8% in school-aged children and 15.6% in preschool-aged children in China [4]. Meanwhile, the incidence of metabolic diseases associated with obesity is higher in children, including non-alcoholic fatty liver disease, metabolic syndrome, precocious puberty, and diabetes mellitus [5]. Obesity may induce endocrine disorders, disturbances in glycolipid metabolism, and insulin resistance (IR) [6,7]. Increased adipose tissue deposition promotes the release of inflammatory mediators and free fatty acids, disrupting insulin signaling and reducing insulin sensitivity in tissues such as muscle and liver, thereby triggering IR [8]. Persistent IR may lead to pancreatic β-cell dysfunction and eventually progress to type 2 diabetes [9]. Therefore, investigating the pathological mechanisms and risk factors of obesity and IR is essential for early diagnosis and intervention, and is of great significance for improving the physiological health of children.

Previous studies have investigated the associations between blood lipids and IR in individuals with obesity [10,11]. However, the pathological mechanisms of IR involve multiple systems, and alterations in lipid metabolism alone cannot fully elucidate the pathological mechanisms of IR in obesity. Exploring additional key factors beyond lipids can help optimize early intervention strategies for IR in children with obesity. Vitamin D and insulin-like growth factor-1 (IGF-1) are closely associated with glucose metabolism and insulin signaling regulation. Vitamin D binds to its receptor in the pancreas and upregulates insulin receptor expression, thereby enhancing cellular sensitivity to insulin [12]. IGF-1 can improve insulin resistance by activating insulin receptors, suppressing hepatic glucose production, and promoting pancreatic β-cell proliferation [13].

Abnormal levels of vitamin D and IGF-1 have been observed in children with obesity [14,15]. Vitamin D deficiency is more common in children with overweight or obesity compared with normal-weight individuals [16]. Adipose tissue can sequester vitamin D, thereby reducing circulating concentrations. Additionally, inflammatory factors secreted by adipocytes may interfere with the activity of 1α-hydroxylase in the kidney, thereby affecting the activation of vitamin D [14]. 25-hydroxyvitamin D (25-(OH)D) is the main circulating and storage form of vitamin D activation in the body. It is further converted to the active form ($1\alpha,25(OH)_2D_3$), mainly in the kidney, and participates in multiple physiological processes, including calcium and phosphorus metabolism, immune regulation, and cell differentiation [17,18]. It has been reported that low serum 25-(OH)D levels are a risk factor for IR in type 2 diabetes [19]. However, the association between 25-(OH)D and IR in children with obesity remains to be fully elucidated.

IGF-1 is primarily synthesized in the liver. Its structure is similar to insulin, and it enhances tissue glucose uptake and increases insulin sensitivity by binding to IGF-1 receptors [20]. Additionally, chronic inflammation induced by adipose accumulation may reduce the biological activity of IGF-1 [21]. Some studies have reported that children with obesity exhibit lower IGF-1 levels [15], while others have found increased serum IGF-1 levels compared with lean individuals [22]. Therefore, the relationship between IGF-1 and IR remains controversial and warrants further investigation.

Insulin resistance in children is not only associated with lipid metabolism, but also involves multiple interacting factors. A comprehensive analysis of the associations among lipids, 25-(OH)D, IGF-1, and IR may better reflect the underlying characteristics and clarify the influencing factors of IR in this population. This study aims to explore the correlation between serum 25-(OH)D, IGF-1, blood lipid levels, and IR in children with obesity, thereby providing a reference for clinical prevention and intervention strategies.

2. Methods

2.1 Patients

A total of 125 children with obesity who visited the Department of Pediatrics, The Affiliated Yangming Hospital of Ningbo University between January 2023 and April 2025 were included in a retrospective analysis. The inclusion criteria were as follows: (1) age 5–15 years; (2) children with obesity, defined according to age- and sex-specific body mass index (BMI) criteria for obesity based on Chinese standards [23,24]; and (3) complete clinical data.

Children meeting any of the following criteria were excluded: (1) abnormal liver or kidney function; (2) endocrine diseases associated with IR, such as thyroid dysfunction, Cushing's syndrome, or abnormal growth hormone secretion; (3) presence of malignancies, immune or allergy-related diseases, including asthma; (4) history of hypoglycemic drug use, including metformin or insulin within three months; (5) intake of vitamin D supplements within three months; and (6) significant weight loss or history of weight loss surgery within six months. This study was approved by the institutional Ethics Committee of The Affiliated Yangming Hospital of Ningbo University (No.2025-09-010) and conducted in accordance with the Declaration of Helsinki. Given that this was a retrospective study without intervention and that only anonymized medical records and clinical data were analyzed, informed consent was waived by The Affiliated Yangming Hospital of Ningbo University.

2.2 Children Grouping

Fasting venous blood samples were collected from all children. Fasting blood glucose was measured using an automatic biochemical analyzer (LABOSPECT 008AS, Hitachi, Tokyo, Japan), and fasting insulin was determined using an automatic chemiluminescence immunoassay analyzer (I2000, Abbott, North Chicago, IL, USA). The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using the formula:

HOMA-IR = (Fasting blood glucose [mmol/L] × Fasting insulin [μU/mL]) / 22.5.

Previous studies have reported that a HOMA-IR cut-off value of 3.16 is appropriate for diagnosing IR in children (mean age 12.04 years) [25], and this criterion has been adopted in other studies [26,27]. Accordingly, IR was defined as HOMA-IR ≥3.16 in this study. Based on insulin sensitivity, the children were divided into two groups: the insulin-sensitive group (n = 56, HOMA-IR <3.16) and the insulin-resistant group (n = 69, HOMA-IR ≥3.16). Baseline characteristics of the children were collected, including age, BMI, sex, family history of diabetes mellitus (defined as diabetes mellitus in a first-degree relative), sampling season, Tanner stage, and physical activity. Sampling seasons were categorized as Spring (March–May), Summer (June–August), Autumn (September–November), and Winter (December–February). Moderate physical activity was defined as at least 60 minutes of aerobic exercise, ball sports, and outdoor games, or achieving a rating of perceived exertion (RPE) score of 4–5 points on the modified Borg 10-point scale after physical activity. Fig. 1 illustrates the processes of participant selection and grouping.

2.3 Detection of 25-(OH)D, IGF-1, and Blood Lipid Levels

Serum 25-(OH)D, IGF-1, and blood lipid levels were measured concurrently with fasting blood glucose and insulin. Blood lipids were analyzed using an automatic biochemical analyzer, including high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and total cholesterol (TC).

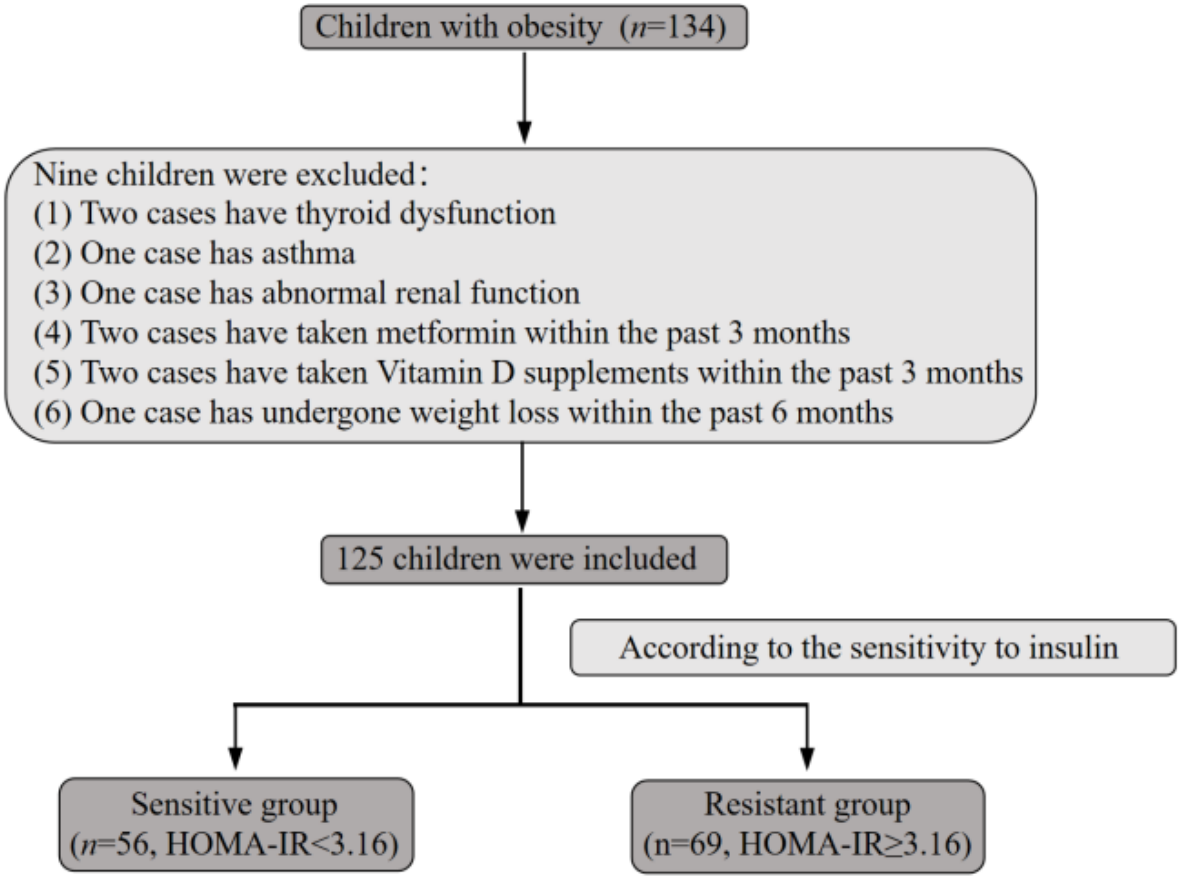

Fig. 1. Flowchart of participant selection and grouping. Abbreviation: HOMA-IR, Homeostasis Model Assessment of Insulin Resistance.

Serum 25-(OH)D and IGF-1 levels were determined using a chemiluminescence immunoassay according to the manufacturer's instructions of the immunoassay analyzer (iFlash 3000; Shenzhen YHLO Biotech Co., Ltd., Shenzhen, China).

2.4 Statistical Analysis

Statistical analyses were performed using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous data was assessed using the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), while skewed data are expressed as median (interquartile range). Independent-samples *t*-test and Mann-Whitney *U* test were used to compare intergroup differences for normally and non-normally distributed data, respectively. Categorical variables are presented as frequencies (percentages), and comparisons between groups were conducted using the chi-square (χ^2) test or Fisher's exact test. Factors influencing IR were analyzed using binary logistic regression. Specifically, univariate logistic regression analysis was performed to evaluate the association of each variable with IR. Variables with $p < 0.05$ in the univariate analysis were included in the multivariate logistic regression model (entry method: enter). Before multivariate analysis, variance inflation factors (VIFs) of all variables were <5, indicating no significant multicollinearity. Receiver operating characteristic (ROC) curves were generated to analyze the discriminatory performance of the indicators for IR. A p-value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline Characteristics of the Participants

No significant differences were observed between the two groups in age, BMI, sex, fasting blood glucose, family history of diabetes mellitus, sampling season, Tanner stage, or moderate physical activity (>3 times/week) ($p > 0.05$). The fasting insulin and HOMA-IR levels in the insulin-resistant group were significantly higher than those in the insulin-sensitive group ($p < 0.001$) (Table 1).

3.2 Comparison of Serum 25-(OH)D, IGF-1, and Blood Lipid Levels Between the Two Groups

Compared with the insulin-sensitive group, the levels of 25-(OH)D, IGF-1, and HDL-C in the insulin-resistant group were significantly decreased ($p < 0.001$, $p = 0.032$, $p = 0.023$). In contrast, TG and LDL-C levels in the insulin-resistant group were significantly higher than those in the

Table 1. Comparison of baseline characteristics between the two groups.

Variable	Insulin-sensitive group (n = 56)	Insulin-resistant group (n = 69)	Statistic ($t/Z/\chi^2$)	p-value
Age (years), M (Q1, Q3)	11 (9–12)	11 (10–12)	1.581	0.114
BMI (kg/m^2), mean ± SD	25.70 ± 3.01	26.66 ± 3.12	1.738	0.085
Sex (n, %)			0.163	0.686
Female	9 (16.07%)	13 (18.84%)		
Male	47 (83.93%)	56 (81.16%)		
Family history of diabetes (n, %)			0.008	0.928
Yes	7 (12.50%)	9 (13.04%)		
No	49 (87.50%)	60 (86.96%)		
Fasting blood glucose (mmol/L), M (Q1, Q3)	4.99 (4.78–5.22)	5.06 (4.86–5.30)	1.075	0.282
Fasting insulin (μU/mL), M (Q1, Q3)	9.8 (7.9–11.8)	24.5 (18.4–32.4)	9.411	<0.001
HOMA-IR, M (Q1, Q3)	2.15 (1.75–2.71)	5.50 (3.95–7.21)	9.592	<0.001
Sampling season (n, %)			0.288	0.962
Spring	9 (16.07%)	11 (15.94%)		
Summer	21 (37.50%)	26 (37.68%)		
Autumn	18 (32.14%)	20 (28.99%)		
Winter	8 (14.29%)	12 (17.39%)		
Tanner stage (n, %)			1.217	0.749
I	23 (41.07%)	27 (39.13%)		
II	20 (35.71%)	21 (30.43%)		
III	11 (19.64%)	16 (23.19%)		
IV	2 (3.57%)	5 (7.25%)		
Moderate physical activity, >3 times/week (n, %)			2.309	0.129
Yes	32 (57.14%)	30 (43.48%)		
No	24 (42.86%)	39 (56.52%)		

Abbreviations: BMI, body mass index; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; M, median; Q1, first quartile; Q3, third quartile; SD, standard deviation.

insulin-sensitive group ($p < 0.001$). No significant difference was observed in TC levels between the two groups ($p = 0.334$) (Table 2).

3.3 Analysis of Influencing Factors of IR in Children With Obesity

Given the clinical applicability and interpretability, IGF-1 was converted into categorical data based on the cut-off value (238.68). Univariate logistic regression analysis showed that 25-(OH)D (odds ratio [OR] = 0.924, 95% confidence interval [CI]: 0.875–0.975, $p = 0.004$), IGF-1 >238.68 (OR = 0.293, 95% CI: 0.120–0.718, $p = 0.007$), TG (OR = 7.757, 95% CI =3.155–19.067, $p < 0.001$), and LDL-C (OR = 3.299, 95% CI: 1.900–5.729, $p < 0.001$) were associated with IR in children with obesity.

Variables with statistical significance in the univariate analysis were included in the multivariate logistic regression. The results indicated that independent influencing factors of IR in children with obesity included 25-(OH)D (OR = 0.934, 95% CI: 0.877–0.995, $p = 0.035$), IGF-1 >238.68 (OR = 0.303, 95% CI: 0.103–0.894, $p = 0.031$), TG (OR = 3.979, 95% CI: 1.461–10.835, $p = 0.007$), and LDL-C (OR = 2.625, 95% CI: 1.398–4.928, $p = 0.003$) (Table 3).

Given that 25-(OH)D levels may be influenced by sampling season, Tanner stage, and physical activity, an additional multivariate logistic regression analysis was performed to investigate whether these factors affected the association between 25-(OH)D and IR. After adjustment for sampling season, Tanner stage, and physical activity, 25-OH(D) remained an independent influencing factor for IR (OR = 0.920, 95% CI: 0.864–0.980, $p = 0.010$) (Table 4).

3.4 ROC Analysis

The ROC analysis demonstrated that the area under the curve (AUC) values of 25-(OH)D, IGF-1, TG, LDL-C, and the combined indicator were 0.692, 0.612, 0.775, 0.747, and 0.856, respectively ($p < 0.001$, $p = 0.025$, $p < 0.001$, $p < 0.001$, $p < 0.001$) (Table 5 and Fig. 2).

4. Discussion

Obesity has become a major global public health concern. Diseases associated with overweight and obesity, such as diabetes mellitus, hypertension, and cardiovascular disease, are increasing annually, with a trend toward younger populations [3]. Excessive expansion of adipose tissue in children with obesity can induce IR and impaired glucose tolerance, thereby increasing the risk of early-onset

Table 2. Comparison of serum 25-(OH)D, IGF-1, and blood lipid profiles between the two groups.

Variable	Insulin-sensitive group (n = 56)	Insulin-resistant group (n = 69)	*Z*	*p*-value
25-(OH)D (ng/mL), M (Q1, Q3)	23.20 (19.33–28.10)	19.68 (17.23–22.36)	3.676	<0.001
IGF-1 (μg/L), M (Q1, Q3)	359.84 (265.08–505.29)	302.18 (216.04–462.37)	2.150	0.032
TG (mmol/L), M (Q1, Q3)	0.79 (0.54–1.04)	1.40 (0.90–1.76)	5.283	<0.001
TC (mmol/L), M (Q1, Q3)	4.22 (3.66–4.67)	4.16 (3.68–4.44)	0.966	0.334
HDL-C (mmol/L), M (Q1, Q3)	1.26 (1.12–1.47)	1.11 (0.97–1.43)	2.282	0.023
LDL-C (mmol/L), M (Q1, Q3)	2.43 (2.06–2.95)	3.18 (2.62–3.85)	4.736	<0.001

Abbreviations: 25-(OH)D, 25-hydroxyvitamin D; IGF-1, insulin-like growth factor-1; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, median; Q1, first quartile; Q3, third quartile.

Table 3. Logistic regression analysis of factors associated with IR in children with obesity.

Variable	Univariate analysis					Multivariate analysis				
	β	SE	Wald	OR (95% CI)	*p*-value	β	SE	Wald	OR (95% CI)	*p*-value
Age	0.171	0.095	3.215	1.186 (0.984–1.429)	0.073					
BMI	0.104	0.061	2.911	1.109 (0.985–1.250)	0.088					
Sex (male)	–0.193	0.477	0.163	0.825 (0.324–2.099)	0.686					
Family history of diabetes	0.049	0.539	0.008	1.050 (0.365–3.023)	0.928					
Sampling season										
Spring				1.00 (Reference)	/					
Summer	0.013	0.537	0.001	1.013 (0.354–2.901)	0.981					
Autumn	–0.095	0.555	0.030	0.909 (0.307–2.696)	0.864					
Winter	0.205	0.641	0.102	1.227 (0.350–4.307)	0.749					
Tanner stage										
I				1.00 (Reference)	/					
II	–0.112	0.422	0.070	0.894 (0.391–2.046)	0.792					
III	0.214	0.484	0.196	1.239 (0.480–3.197)	0.658					
IV	0.756	0.883	0.732	2.130 (0.377–12.031)	0.392					
Moderate physical ac -tivity >3 times/week	–0.550	0.363	2.294	0.577 (0.283–1.176)	0.130					
25-(OH)D	–0.079	0.028	8.182	0.924 (0.875–0.975)	0.004	–0.068	0.032	4.463	0.934 (0.877–0.995)	0.035
IGF-1 >238.68	–1.226	0.457	7.212	0.293 (0.120–0.718)	0.007	–1.194	0.552	4.679	0.303 (0.103–0.894)	0.031
TG	2.049	0.459	19.927	7.757 (3.155–19.067)	<0.001	1.381	0.511	7.303	3.979 (1.461–10.835)	0.007
TC	–0.263	0.274	0.924	0.769 (0.450–1.314)	0.336					
HDL-C	–1.222	0.666	3.369	0.295 (0.080–1.086)	0.066					
LDL-C	1.194	0.282	17.976	3.299 (1.900–5.729)	<0.001	0.965	0.321	9.020	2.625 (1.398–4.928)	0.003

Abbreviations: IR, insulin resistance; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol; 25-(OH)D, 25-hydroxyvitamin D; IGF-1, insulin-like growth factor-1; SE, standard error; OR, odds ratio; CI, confidence interval.

type 2 diabetes [28]. Notably, IR developed during childhood may persist long-term and is closely associated with chronic metabolic diseases, including non-alcoholic fatty liver disease and atherosclerosis [28]. Therefore, identifying factors associated with IR in children with obesity is of significant importance for early recognition and timely intervention.

In this study, among children with obesity, 25-(OH)D, IGF-1 >238.68, TG, and LDL-C were significantly associated with IR. ROC analysis further indicated that the combined detection of these indicators provided better discriminatory performance for IR than any individual indicator alone. A total of 125 children with obesity were included in this study. However, the proportion of girls was relatively low (22/125, 17.6%). The participants were recruited from the pediatric department of the hospital, where boys constitute a higher proportion among children with obesity attending outpatient clinics. One possible explanation is that girls with obesity may be more likely to seek care in endocrinology or gynecology departments. Although the proportion of girls in this study was lower than the natural population distribution, it reflects the actual gender composition of patients visiting our department. This imbalance may introduce potential gender bias. Therefore, future studies should

Table 4. Multivariate logistic regression analysis of the association between 25-(OH)D and IR after adjustment for sampling season, Tanner stage, and physical activity.

Variable	β	SE	Wald	OR (95% CI)	*p*
Sampling season					
Spring				1.00 (Reference)	–
Summer	–0.074	0.573	0.017	0.929 (0.301–2.867)	0.898
Autumn	–0.160	0.592	0.073	0.852 (0.265–2.733)	0.787
Winter	–0.023	0.689	0.001	0.977 (0.253–3.776)	0.973
Tanner stage					
I				1.00 (Reference)	–
II	–0.028	0.443	0.004	0.972 (0.407–2.318)	0.948
III	0.412	0.525	0.615	1.510 (0.536–4.256)	0.436
IV	0.816	0.917	0.793	2.262 (0.386–13.237)	0.365
Moderate physical activity (>3 times/week)	0.035	0.424	0.007	1.036 (0.450–2.383)	0.934
25-(OH)D	–0.083	0.030	7.727	0.920 (0.864–0.980)	0.010

Abbreviations: IR, insulin resistance; 25-(OH)D, 25-hydroxyvitamin D; OR, odds ratio; CI, confidence interval.

Table 5. ROC analysis of 25-(OH)D, IGF-1, TG, and LDL-C for discrimination of IR in children with obesity.

Variable	AUC	95% CI	*p*-value	Sensitivity	Specificity	Cut-off value
25-(OH)D	0.692	0.597–0.786	<0.001	0.710	0.661	20.825
IGF-1	0.612	0.514–0.710	0.025	0.362	0.857	238.680
TG	0.775	0.693–0.857	<0.001	0.681	0.768	1.055
LDL-C	0.747	0.660–0.833	<0.001	0.594	0.839	3.075
Combined indicator	0.856	0.786–0.925	<0.001	0.739	0.893	/

Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; IR, insulin resistance; CI, confidence interval; 25-(OH)D, 25-hydroxyvitamin D; IGF-1, insulin-like growth factor-1; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol.

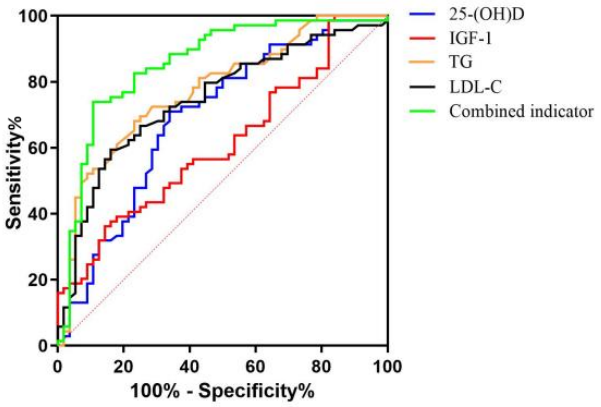

Fig. 2. ROC curves of 25-(OH)D, IGF-1, TG, LDL-C and Combined indicator for discrimination of IR in children with obesity. Abbreviations: ROC, receiver operating characteristic; IR, insulin resistance; 25-(OH)D, 25-hydroxyvitamin D; IGF-1, insulin-like growth factor-1; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol.

aim to increase the proportion of female participants to reduce such bias. Additionally, this study focused on children aged 5–15 years. This age encompasses a crucial developmental period from preschool to adolescence and represents a window for early identification and intervention of IR. Moreover, children in this age group generally have sufficient cognitive ability and cooperation during clinical examinations. Several previous studies have also selected children within this age range as research subjects [29,30].

In this study, compared with the insulin-sensitive group, the insulin-resistant group showed a slight increase in fasting blood glucose without statistical significance; however, fasting insulin levels were significantly elevated. The primary reason may be that excessive adipose tissue accumulation interferes with insulin signaling pathways, leading to reduced insulin sensitivity. Consequently, pancreatic β cells increase insulin secretion to maintain glucose homeostasis. Moreover, hyperinsulinemia may further exacerbate IR [31]. Niu et al. [26] reported similar findings in children and adolescents with obesity. For these children with IR, close monitoring and early intervention are necessary to prevent progression to diabetes [26].

25-(OH)D is the main storage form of vitamin D. The relationship between 25-(OH)D and obesity has been investigated in previous studies. Compared with children of healthy weight, serum 25-(OH)D levels in overweight children are decreased [32]. Vitamin D deficiency may lead to various diseases, such as growth retardation, osteomala-

cia, and metabolic disorders [33,34]. In this study, serum 25-(OH)D levels in the IR group were significantly lower than those in the insulin-sensitive group among children with obesity. Low 25-(OH)D was identified as a risk factor for IR in this population. A study reported that serum 25-(OH)D was negatively correlated with IR in children [35]. These findings are consistent with the findings of the present study.

Mechanistically, 25-(OH)D may suppress pro-inflammatory cytokine production and regulate cellular immunity through pathways such as the nuclear factor kappa-B (NF-κB) and mitogen-activated protein kinase (MAPK) signaling pathways, thereby improving IR [36]. *In vitro* experiments have shown that 1,25-$(OH)_2D_3$ alleviates endoplasmic reticulum stress by inhibiting the protein kinase-like ER kinase (PERK)-activating transcription factor 4 (ATF4)-C/enhancer-binding protein (EBP) homologous protein (CHOP) pathway, thereby protecting pancreatic β cells from damage [37]. Moreover, vitamin D can promote adiponectin secretion by adipocytes, and adiponectin has a beneficial effect on improving IR [38].

IGF-1 is an insulin-like molecule that participates in growth regulation, cell proliferation, protein synthesis, nervous system development, and pancreatic islet proliferation [20]. A previous study has reported that IGF-1 levels are lower in children with obesity compared with those of normal weight [39]. In the present study, IGF-1 levels are lower in the insulin-resistant group than in the insulin-sensitive group. IGF-1 >238.68 was identified as an independent influencing factor of IR in children with obesity. However, it should be noted that the AUC of IGF-1 was 0.612, indicating limited discriminatory performance for IR. Therefore, in clinical practice, IGF-1 should be combined with other indicators to improve discriminatory performance. Previous studies have shown that weight loss increases IGF-1 levels and reduces IR in children with obesity [40], supporting our findings. Mechanistically, IGF-1 may improve pancreatic β-cell viability, promote insulin secretion, and regulate glucose metabolism through activation of insulin receptor substrate 1 (IRS1)/phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt)/forkhead box protein O1 (FOXO1) pathway [13].

Obesity is closely associated with dysregulated lipid metabolism. Excessive accumulation of adipose tissue activates lipolytic pathways, leading to elevated levels of circulating free fatty acids. These elevated free fatty acids are transported to the liver, promoting TG synthesis, upregulating the expression of genes associated with LDL-C synthesis, and downregulating proteins that mediate HDL-C reverse transport (e.g., adenosine triphosphate-binding cassette transporter A1 and scavenger receptor class B type 1) [41]. Moreover, obesity is characterized by increased macrophage infiltration into adipose tissue, which triggers a chronic low-grade inflammatory cascade and the release of pro-inflammatory cytokines. These mediators disrupt insulin signaling pathways in peripheral target organs, thereby reducing insulin sensitivity and contributing to IR [8].

In the present study, children with IR exhibited significantly higher TG and LDL-C levels and lower HDL-C levels compared with insulin-sensitive counterparts. Multivariate logistic regression analysis further identified TG and LDL-C as independent risk factors for IR in children with obesity. Consistent with our findings, a previous study among residents aged ≥40 years has demonstrated that individuals with IR exhibit elevated TG, TC, and LDL-C levels and reduced HDL-C levels, with these lipid parameters showing significant correlations with fasting insulin concentrations [42]. However, no significant association between TC and IR was observed in this study, which may reflect differences in research subjects, as our cohort was restricted to children with obesity.

This study had several limitations. First, the samples were obtained from a single center, and the sample size was relatively small. Multi-center prospective studies with larger clinical cohorts are needed in the future to validate these findings. Second, the number of female participants was limited, and our results may therefore be subject to gender bias. Increasing the representation of female participants in future studies is necessary to mitigate this bias. Third, given that a small sample size reduces the robustness and performance of models, we did not further construct a model for IR. Such clinical models should be constructed in subsequent research using large sample sizes.

5. Conclusion

Among children with obesity, 25-(OH)D, IGF-1, TG, and LDL-C were associated with IR. Compared with insulin-sensitive children, the levels of 25-(OH)D, IGF-1, and HDL-C were decreased in children with IR, while TG and LDL-C levels were increased. The combined assessment of these indicators demonstrated better discriminative performance for IR than any individual indicator alone.

Key Points

- The levels of 25-(OH)D, IGF-1, and HDL-C were lower in the insulin-resistant group, while TG and LDL-C levels were higher compared with the insulin-sensitive group among children with obesity.
- 25-(OH)D, IGF-1 >238.68, TG, and LDL-C were independent influencing factors of IR in children with obesity.
- The combination of 25-(OH)D, IGF-1, TG, and LDL-C demonstrated superior discriminative performance for IR compared with individual indicators in children with obesity.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

ZFC, KJY and YL designed the research study and wrote the first draft. ZFC and YL performed the research. ZFC and YL analyzed the data. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the institutional Ethics Committee of The Affiliated Yangming Hospital of Ningbo University (No.2025-09-010) and conducted in accordance with the Declaration of Helsinki. Given that this was a retrospective study without intervention and that only anonymized medical records and clinical data were analyzed, informed consent was waived by The Affiliated Yangming Hospital of Ningbo University.

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Conflicts of Interest

The authors declare no conflicts of interest.

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