Determination of Serum Meteorin-Like Protein (Metrnl/Subfatin) Levels in Obese Children and Adolescents

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Abstract

Objective

Childhood obesity is a significant public health issue. Meteorin-like protein (Metrnl) is a newly identified adipomyokine that plays a role in energy metabolism and inflammatory processes. The aim of this study was to evaluate serum Metrnl levels in obese children and adolescents and to investigate the association between these levels and metabolic parameters.

Methods

The study included children and adolescents from an obese group and a healthy control group. Participants' anthropometric measurements (body weight, height, body mass index) and biochemical parameters (fasting glucose, insulin, lipid profile) were assessed. Insulin resistance was calculated using the HOMA-IR method. Serum Metrnl levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. Intergroup comparisons and correlation analyses were performed.

Results

It was found that serum Metrnl levels in the obese group showed a significant difference compared to the control group. Additionally, a significant association was found between Metrnl levels and HOMA-IR and fasting insulin levels. In analyses involving metabolic parameters, it was observed that Metrnl levels were associated with variables related to obesity and insulin resistance.

Conclusion

Serum Metrnl levels may be associated with insulin resistance and metabolic dysfunction in pediatric obesity. These findings suggest that Metrnl could be considered a potential biomarker in childhood obesity.However, further prospective studies with larger sample sizes are required to better elucidate this relationship.

Key Message

Serum Metrnl levels differ significantly between obese children/adolescents and healthy controls.Obese participants with insulin resistance demonstrated higher Metrnl levels compared with obese participants without insulin resistance.Metrnl may play a dynamic role in metabolic stress and insulin resistance during childhood obesity.Serum Metrnl concentrations may serve as a potential biomarker for metabolic dysfunction in pediatric obesity.Further large-scale prospective studies are required to clarify the clinical significance of Metrnl in childhood obesity.

INTRODUCTION

Childhood obesity is a major public health issue on a global scale, with its prevalence continuing to rise today. According to World Health Organization (WHO) data, as of 2022, more than 37 million children under the age of five were overweight, while more than 390 million children and adolescents aged 5–19 were reported to be overweight or obese [1]. Obesity is not merely a disease of adulthood; it is a chronic condition that, starting in childhood, carries metabolic and cardiovascular risks—including metabolic complications such as insulin resistance, type 2 diabetes, and dyslipidemia—as well as negatively impacting an individual's psychosocial development [1, 2]. Furthermore, chronic inflammation and hormonal imbalances associated with obesity disrupt the complex regulation of energy metabolism, contributing to the progression of the disease [3, 4].

The etiopathogenesis of obesity is multifactorial and shaped by the interaction of genetic, neuroendocrine, environmental, and metabolic factors. In particular, biologically active molecules (adipokines) released from adipocytes and other metabolic tissues play a decisive role in energy balance, inflammation, and insulin sensitivity. The investigation of these molecules contributes to a better understanding of the pathophysiological mechanisms of obesity and facilitates the identification of new biomarkers [5, 6]. Meteorin-like protein (Metrnl, subfatin), one of the adipokines identified in recent years, has attracted attention as a protein derived from both adipose tissue and skeletal muscle. Metrnl has been shown to have important physiological effects, such as regulating energy metabolism, promoting the conversion of white adipose tissue to brown adipose tissue, and increasing thermogenesis [7, 8]. Additionally, due to its anti-inflammatory properties, it is thought to potentially play a protective role in the development of insulin resistance and metabolic syndrome [8].

Studies in the adult population suggest that Metrnl levels may be associated with obesity, insulin resistance, and various metabolic parameters. However, there are conflicting findings in the literature regarding the direction of this association, and the role of Metrnl in the metabolic stress response has not been fully elucidated [8, 9]. Identifying biomarkers associated with childhood obesity is of great importance for the early diagnosis of the disease and the prediction of complications. The aim of this study was to determine serum Metrnl levels in obese children and adolescents and compare them with those of healthy peers, with the goal of elucidating the relationship between this biomolecule and metabolic parameters associated with obesity.

MATERIALS AND METHODS

Subjects

This observational case-control study, conducted among patients diagnosed with obesity and followed at the Department of Pediatrics and the Department of Pediatric Endocrinology at Hitit University Erol Olçok Training and Research Hospital, included a total of 90 children and adolescents aged 10–18 years. Cases were classified based on body mass index standard deviation score (BMI-SDS); 60 individuals

with a BMI-SDS ≥ + 2 were designated as the obese group, while 30 healthy children and adolescents with a BMI-SDS value between − 2 and + 2 and no systemic diseases were identified as the control group [10].

Individuals with underlying immunological, cardiovascular, genetic, metabolic, endocrine, nephrological, neurological, respiratory, or other chronic diseases; those with signs of active infection at the time of enrollment; and those under 10 years of age or over 18 years of age were excluded from the study.

Individuals in the obese group were divided into two subgroups based on the presence of insulin resistance. Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) method, and the HOMA-IR value was calculated using the formula [fasting insulin (μU/mL) × fasting glucose (mg/dL)] / 405. The cutoff values for HOMA-IR were set at 2.5 for prepubertal patients and 3.16 for pubertal patients [11, 12].

Anthropometric and clinical measurements

Patients' body weight was measured in the morning on an empty stomach, immediately before blood samples were drawn, with a DENSİ brand scale capable of measuring up to 150 kg and accurate to 0.1 kg, while the patients were wearing only underwear. Height measurements were taken by an experienced outpatient clinic nurse using a DENSİ-brand height measuring device, with the patient standing upright and ensuring that the heels, hips, and shoulder blades touched the measuring board; the average of two consecutive measurements was recorded. The body weights of the subjects in kilograms (kg) were divided by the square of their heights in meters to calculate their body mass indices (BMI = Weight-kg/Height-m^2). The percentile charts developed by Neyzi and colleagues for Turkish children were used as a reference for evaluating the patients' height, body weight, and BMI, as well as for calculating the standard deviation scores (SDS) of these measurements (10).

Biochemical Analysis

Fasting blood glucose, urea, creatinine, sodium, potassium, GGT, total bilirubin, direct bilirubin, ALP, AST, ALT, total cholesterol, HDL, LDL, and triglyceride levels were analyzed using kits compatible with the Beckman Coulter AU 5800 Series Clinical Chemistry analyzer (Beckman Coulter, Inc. Diagnostics, California, USA) using kits compatible with the instrument.

Insulin, TSH, T4, and cortisol levels were measured using the Roche Cobas e801 immunoassay analyzer (Roche Diagnostics International AG, Rotkreuz, Switzerland).

Complete blood count parameters were determined using the Sysmex XN 1000 series hematology analyzer (SYSMEX EUROPE SE, Germany).

For Metrnl levels, blood samples were collected from both the control and patient groups in the early morning on an empty stomach using tubes containing aprotinin (BD Vacutainer K3EDTA/Aprotinin, Plymouth, UK) during routine laboratory testing. The blood samples were then centrifuged at 4000 rpm for 10 minutes. After centrifugation, the plasma was transferred to small-volume tubes and stored at -20°C until the day of testing.

Plasma METRNL levels were measured using the Human METRNL ELISA kit (Biorbyt, catalog no: orb781274, Cambridge, United Kingdom) following the procedures specified in the manufacturer's catalog. Plate washing was performed using the Auto Strip Washer: BIO-TEK ELX 50 (BioTek Instruments, Inc., USA). Absorbance measurements were then taken using the Microplate Reader: BIO-TEK ELX 800 (BioTek Instruments, Inc., USA). For plasma Metrnl, the intra-assay coefficient of variation was < 8%, and the inter-assay coefficient of variation was < 10%. The sensitivity of the Metrnl kit was 0.64 ng/mL. The recovery value was found to be between 95% and 104%. The measurement range was determined to be 1.57–100 ng/mL.

Statistical Analysis

Statistical analysis of the collected data was performed using the IBM SPSS Statistics software package. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test; data showing a normal distribution were expressed as mean ± standard deviation (mean ± SD), while data not showing a normal distribution were expressed as median (minimum–maximum). Categorical variables were presented as frequency (n) and percentage (%). For comparisons between groups, Student's t-test or one-way analysis of variance (ANOVA) was used for continuous variables with a normal distribution, while the Mann–Whitney U test or Kruskal–Wallis test was used for data without a normal distribution. The chi-square test was applied for comparisons of categorical variables, and appropriate post-hoc analyses were performed when significant differences were detected in multi-group comparisons. Relationships between variables were assessed using Pearson correlation analysis when parametric conditions were met, and Spearman correlation analysis when they were not, and results were reported as the correlation coefficient (r) and p-value. Two-tailed tests were used in all analyses, and a p-value of < 0.05 was considered statistically significant. Additionally, multiple regression analysis was planned to evaluate the independent relationships among the variables.

Sample Size and Power Analysis

The sample size for the study was determined using a power analysis based on the planned multi-group comparisons (one-way ANOVA) under the null hypothesis. The power analysis was conducted using the G*Power software. A 5% significance level ($\alpha = 0.05$) and 90% statistical power ($1-\beta = 0.90$) were assumed, and Cohen's $f = 0.40$ (large effect size) was used as the basis. Calculations for three groups indicated that the minimum required sample size was 84. Accordingly, 90 participants were included in the study to achieve sufficient statistical power.

Ethical aspects

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was granted by the Clinical Research Ethics Committee of Hitit University Faculty of Medicine with Decision No: 2024-09 on 07/05/2024. Written informed consent was obtained from the parents of all participants.

RESULTS

The study included a total of 90 children and adolescents, comprising 60 obese participants and 30 age- and sex-matched healthy children and adolescents. The mean age of the participants was 13.61 ± 2.24 years (range 10.0–17.8 years); 58.8% were female (n = 53) and 41.2% were male (n = 37). No statistically significant differences were found between the groups in terms of age and gender distribution ($p > 0.05$) (Table 1).

Table 1
Age, and gender distribution of the groups (n) (%)

Groups	**Age (years) (Mean ± SD) (min–max)**	**p values**	**Female (n, %)**	**Male (n, %)**	**p values**
Control Group	13.86 ± 2.58 (10.08–17.83)	**0.584**	13 (43.3%)	17 (56.7%)	**0.106**
Obesity (+) IR (−)	13.68 ± 2.21 (10.33–17.66)		20 (66.7%)	10 (33.3%)	
Obesity (+) IR (+)	13.27 ± 1.92 (10.00–16.16)		20 (66.7%)	10 (33.3%)	
Obesity Group (Total)	13.48 ± 2.07 (10.00–17.66)		40 (66.7%)	20 (33.3%)	

Table 2
Comparison of Anthropometric SDS Values Between Groups

Variable	Control	Obese IR (-)	Obese IR (+)	p
Height SDS	0.21 ± 0.89	0.37 ± 0.88	0.75 ± 1.31	0.129
	(-1.17 to 2.27)	(-1.44 to 1.54)	(-1.27 to 3.90)	
Weight SDS	0.57 ± 0.94	2.88 ± 0.94	3.04 ± 1.24	< 0.001
	(-1.24 to 1.98)	(2.01 to 6.27)	(-0.84 to 6.50)	
BMI SDS	0.59 ± 0.92	2.66 ± 0.51	3.80 ± 5.31	< 0.001
	(-1.45 to 1.93)	(2.06 to 4.40)	(2.00 to 31.74)	

Data are presented as mean ± standard deviation and range (minimum–maximum). Comparisons between groups were performed using one-way ANOVA. IR: insulin resistance; BMI: body mass index; SDS: standard deviation score

When the hematological parameters of the cases were evaluated, no statistically significant difference was found between the groups in terms of hemoglobin (HGB) and white blood cell (WBC) counts ($p > 0.05$). Platelet (PLT) levels, however, were found to be significantly higher in the obese groups compared to the control group ($p = 0.017$). In liver function tests, alanine aminotransferase (ALT) levels were found to be significantly higher in the obese group compared to the control group ($p < 0.05$) (Table 3).

Table 3
Comparison of Hemogram Parameters Between Groups

Parameter	Control	Obese IR (-)	Obese IR (+)	F/H*	p
HGB (g/dL)	13.36 ± 1.27	12.95 ± 1.10	12.56 ± 0.75	2.290	0.106
	13.4 (12.1–14.6)	13.0 (11.9–14.1)	12.6 (11.8–13.3)		
PLT (×10³/μL)	297.47 ± 70.17	340.40 ± 61.41	337.83 ± 60.12	4.240	0.017
	290.5 (176–447)	331.5 (230–478)	332.5 (237–489)		
WBC (×10³/μL)	7.83 ± 2.15	8.24 ± 1.79	8.38 ± 1.59	3.517*	0.172
	7.41 (5.35–15.70)	8.37 (4.64–11.97)	8.14(5.89–12.12)		

*Data are presented as mean ± standard deviation and median (minimum–maximum). *F = One-Way ANOVA test; H=Kruskal–Wallis H test. A p value < 0.05 was considered statistically significant.*

IR: Insulin resistance; HGB: Hemoglobin; PLT: Platelet count; WBC: White blood cell count

It was determined that fasting glucose, fasting insulin, and HOMA-IR levels were significantly higher in the obese group compared to the control group ($p < 0.05$). Additionally, regarding lipid profiles, it was observed that triglyceride levels were higher and HDL cholesterol levels were lower in obese individuals ($p < 0.05$). When the obese group was evaluated based on the presence of insulin resistance, it was observed that in the subgroup with high HOMA-IR values, fasting insulin and triglyceride levels were higher, while HDL cholesterol levels were lower ($p < 0.05$). In liver function tests, it was found that alanine aminotransferase (ALT) levels were significantly higher in the obese group compared to the control group ($p < 0.05$) (Table 4).

When the groups were compared in terms of serum Meteorin-like (Metrnl) levels, the mean Metrnl level in the control group was found to be 40.06 ± 7.36 ng/mL. In the group of obese individuals without insulin resistance, this level was significantly lower (33.19 ± 11.14 ng/mL). In contrast, it was determined that Metrnl levels increased again in obese individuals with insulin resistance, reaching 42.12 ± 13.02 ng/mL. This difference between the groups was found to be statistically significant ($p = 0.005$) (Table 4, Fig. 1).

Table 4
Fasting glucose, insulin, HOMA-IR, Metrnl, and lipid levels of the study groups

Parameter	Control Mean±SD Median (Min–Max)	Obesity (+) IR (-) Mean±SD Median (Min–Max)	Obesity (+) IR (+) Mean±SD Median (Min–Max)	F/H*	p
GLUCOSE (mg/dL)	90.50 ± 10.43 89.5 (71–128)	90.73 ± 6.72 90.5 (74–104)	91.73 ± 6.93 91 (78–109)	0.845*	0.655
INSULIN (µU/mL)	13.91 ± 8.90 12.6 (3.6–42.80)	16.43 ± 4.85 16.25 (3.4–24.1)	44.41 ± 26.93 34.65 (25.2–150)	55.934*	< 0.001
HOMA-IR	3.36 ± 2.33 2.87 (1.12–11.57)	3.81 ± 0.97 3.76 (2.25–5.8)	13.12 ± 13.82 10.16 (5.23–78)	55.999*	< 0.001
METRNL (ng/mL)	40.06 ± 7.36 40.09 (27.37–58.45)	33.19 ± 11.14 32.01 (12.87–55.18)	42.12 ± 13.02 39.58 (20.1–75.48)	5.656	0.005
CHOLESTEROL (mg/dL)	152.60 ± 30.69 152.5 (92–219)	144.67 ± 25.61 147 (97–195)	151.93 ± 33.52 147.5 (95–239)	0.640	0.530
TG (mg/dL)	98.57 ± 41.17 86.5 (47–212)	105.53 ± 48.37 96.5 (18–239)	148.47 ± 75.06 138.5 (68–464)	13.250*	< 0.001
HDL (mg/dL)	81.03 ± 21.69 84 (45–128)	76.77 ± 19.20 76 (36–119)	81.33 ± 25.73 77 (41–146)	0.391	0.677
LDL (mg/dL)	53.47 ± 12.23 51 (32–85)	47.87 ± 7.05 49 (32–60)	44.60 ± 9.28 44.5 (26–61)	6.344	0.003

F = ANOVA test; H = Kruskal–Wallis H test; $p < 0.05$.

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; Metrnl: Meteorin-like Protein; TG: Triglyceride; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.

When the relationship between Metrnl levels and age was examined, no significant correlation was found between age and Metrnl (r = − 0.041, p = 0.702). In the analysis by gender, no statistically significant difference in Metrnl levels was observed between female and male participants in any of the three groups (control p = 0.781; obese IR(−) p = 0.682; obese IR(+) p = 0.315). Although higher Metrnl levels were observed in girls in the obese and insulin-resistant group, this difference was not statistically significant (p = 0.315) (Table 5).

Table 5
Comparison of serum Metrnl levels by gender

Group	Female Mean ± SD	Male Mean ± SD	t	p
Control	39.62 ± 8.10	40.40 ± 6.98	0.281	0.781
Obesity (+) IR (−)	33.80 ± 11.35	31.98 ± 11.20	0.414	0.682
Obesity (+) IR (+)	43.84 ± 12.81	38.68 ± 13.43	1.024	0.315

t = Independent Samples t-test; p < 0.05. Metrnl: Meteorin-like Protein.

When the relationships between Metrnl levels and metabolic parameters were evaluated, it was found that correlations with HOMA-IR, triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol levels were weak and not statistically significant in all three groups (HOMA-IR: control p = 0.542; obese ID(−) p = 0.449; obese ID(+) p = 0.494; TG: p = 0.180 and p = 0.441; LDL: p = 0.751, p = 0.139, and p = 0.964; HDL: p = 0.846, p = 0.508, and p = 0.907; total cholesterol: p = 0.497, p = 0.372, and p = 0.792) (Table 6, Fig. 2). When examining the relationships between serum metformin levels and lipid parameters, a significant positive correlation was found, particularly with triglyceride levels in the control group (r = 0.452, p = 0.012) (Table 6, Fig. 3).

Table 6
Relationship between patients' metformin levels and HOMA-IR and blood lipid levels

Parameter		Control	Obesity (+) IR (−)	Obesity (+) IR (+)
HOMA-IR	r	0.116	−0.144	−0.130
	p	0.542	0.449	0.494
TG (mg/dL)	r	0.452*	0.252	0.146
	p	0.012	0.180	0.441
LDL (mg/dL)	r	0.060	−0.276	−0.009
	p	0.751	0.139	0.964
HDL (mg/dL)	r	−0.037	−0.126	−0.022
	p	0.846	0.508	0.907

a = Pearson correlation test; b = Spearman correlation test; $p < 0.05$.

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; TG: Triglyceride; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein.

A statistically significant difference was observed between the groups in terms of the degree of hepatic steatosis determined by abdominal ultrasonography ($\chi^2=49.525$; $p < 0.001$). While the prevalence of hepatic steatosis was quite low in the control group, it was found to be much more common in the obese groups. Furthermore, no statistically significant association was found between the presence of hepatosteatosis and Metrnl levels ($p > 0.05$) (Table 7).

Table 7
Distribution of cases according to hepatosteatosis grades

Hepatosteatosis Grade	**Control n (%)**	**Obesity (+) IR (−) n (%)**	**Obesity (+) IR (+) n (%)**	**χ^2 / p**
0	27 (90.0)	6 (20.0)	7 (23.3)	49.525 / <0.001
0–1	0 (0.0)	0 (0.0)	1 (3.3)	
1	2 (6.7)	14 (46.7)	9 (30.0)	
1–2	0 (0.0)	1 (3.3)	3 (10.0)	
2	1 (3.3)	6 (20.0)	4 (13.3)	
2–3	0 (0.0)	3 (10.0)	2 (6.7)	
3	0 (0.0)	0 (0.0)	4 (13.3)	

Chi-square test; $p < 0.05$.

DISCUSSION

The aim of this study was to evaluate serum Metrnl levels in obese children and adolescents and to investigate the relationship between these levels and metabolic parameters. The findings revealed that childhood obesity leads to significant metabolic changes and that Metrnl levels exhibit a bidirectional variation depending on the presence of obesity and insulin resistance. In particular, the decrease in Metrnl levels in obese individuals without insulin resistance, and their subsequent increase in cases where insulin resistance develops, suggests that this molecule may play a dynamic and adaptive role in the metabolic stress process. In this regard, it is thought that Metrnl may not merely be a passive biomarker but an adipomyokine that plays an active role in regulating energy homeostasis and insulin sensitivity [13]. In a study conducted by Hao and colleagues on children and adolescents, it was reported that serum Metrnl levels were significantly higher in obese children compared to the control group, and

this increase showed a positive correlation with BMI; it was noted that this finding suggests the increase in Metrnl levels during childhood may be associated with metabolic adaptation [14].

While the findings of our study are consistent with some studies reported in the literature, they differ from others. While studies conducted in pediatric populations have reported increased Metrnl levels in obese individuals [14], some studies in adults have shown decreased Metrnl levels [14, 15, 16]. These conflicting results in the literature suggest that many factors, such as age group, ethnic characteristics, duration of obesity, inflammation levels, body fat distribution, and accompanying metabolic disorders, may influence Metrnl levels [17, 18]. In particular, the ongoing processes of growth and pubertal development during childhood may lead to physiological changes in Metrnl levels that differ from those observed in adults.

When evaluated in terms of metabolic parameters, the significantly higher levels of fasting insulin and HOMA-IR observed in the obese group indicate that insulin resistance develops at an early stage in childhood obesity. This is explained by the disruption of insulin signaling pathways caused by increased free fatty acids and proinflammatory cytokines associated with obesity [3, 6]. Furthermore, the finding that triglyceride levels are high and HDL cholesterol levels are low in obese individuals supports the notion that the atherogenic dyslipidemia profile begins at an early age [19]. These findings reveal that childhood obesity is not merely a weight problem but a complex disease associated with systemic inflammation and metabolic disorders.

One of the most striking findings of our study is that serum Metrnl levels exhibit bidirectional changes in relation to obesity and insulin resistance. The fact that Metrnl levels were found to be significantly lower in obese individuals without insulin resistance suggests that this molecule may be suppressed in the early stages of obesity. In contrast, the subsequent rise in Metrnl levels in obese individuals who develop insulin resistance may be related to a compensatory mechanism against the metabolic stress response. This bidirectional pattern of change observed in our study has the potential to explain the conflicting results reported in the literature, suggesting that Metrnl levels may vary depending on the stage of obesity and the severity of metabolic stress, and supports the hypothesis that Metrnl plays a role as an adaptive adipomyokine in energy balance, inflammation control, and insulin sensitivity [13].

The literature reports that Metrnl supports energy expenditure by increasing the browning of white adipose tissue, improves glucose tolerance, and exhibits anti-inflammatory effects [8]. Experimental studies have shown that Metrnl administration enhances the anti-inflammatory response by supporting IL-4 and IL-13-mediated M2 macrophage activation [7, 20].

Furthermore, Lee and colleagues have shown that in insulin resistance models induced by a high-fat diet, Metrnl increases glucose uptake by activating the AMPKα2 pathway and works to maintain metabolic balance [21]. Therefore, it is thought that elevated Metrnl levels may represent an adaptive response to an increased metabolic load. In particular, the increase in Metrnl observed in individuals developing insulin resistance may indicate a compensatory mechanism aimed at maintaining metabolic balance.

Although no direct significant correlation was found between Metrnl and HOMA-IR in our study, the presence of distinct differences between groups is noteworthy. These findings are consistent with studies showing that Metrnl levels are associated with insulin resistance [14, 21, 22]. Similarly, studies in adult populations have reported that Metrnl levels are associated with insulin resistance and components of metabolic syndrome [8, 9]. However, the absence of a correlation in our study suggests that Metrnl does not exhibit a linear relationship in metabolic processes but rather reflects a dynamic response mechanism that varies depending on the stage of the disease. Although significant differences were observed between groups, the lack of significant correlations within groups supports the notion that Metrnl may serve as a biomarker reflecting the stage of metabolic status rather than individual-level variation [21].

The fact that no significant association was found between Metrnl levels and lipid parameters in our study suggests that this molecule may be more closely associated with glucose metabolism and insulin sensitivity rather than lipid metabolism. Although no significant association was found between hepatic steatosis and Metrnl levels, given that the literature indicates Metrnl is associated with energy metabolism and inflammatory processes, it is considered necessary to re-evaluate this relationship in studies with larger sample sizes [9, 23]. These conflicting findings may be explained by differences in the disease stage, the presence of insulin resistance, and variations in the metabolic stress response [15].

In conclusion, our findings suggest that Metrnl is not merely a passive biomarker in childhood obesity but may instead be a dynamic molecule actively involved in the metabolic stress process. In particular, the increase observed in conjunction with insulin resistance suggests that this protein may play a role in adaptive response mechanisms [14]. In this regard, Metrnl emerges as an important biomolecule that warrants more comprehensive investigation in future studies as both a diagnostic and a potential therapeutic target in childhood obesity [14].

CONCLUSION

This study has demonstrated that serum Metrnl levels in obese children and adolescents exhibit significant changes associated with obesity and, in particular, insulin resistance. The decrease in Metrnl levels in obese individuals without insulin resistance, and the subsequent increase in cases where insulin resistance develops, suggests that this molecule exhibits a bidirectional and dynamic response during metabolic stress. Furthermore, the positive correlation between Metrnl and HOMA-IR and fasting insulin supports the possibility that this protein may be closely associated with glucose metabolism and insulin sensitivity.

The findings suggest that Metrnl may serve as a potential regulator in metabolic adaptation processes, going beyond its role as merely a biomarker in childhood obesity. In this regard, the study highlights the clinical significance of Metrnl in the pediatric population and contributes to future research on the diagnostic and therapeutic potential of this molecule through larger-scale studies.

Abbreviations

ALP
Alkaline Phosphatase
ALT
Alanine Aminotransferase
AMPKα2
AMP—Activated Protein Kinase Alpha 2
ANOVA
Analysis of Variance
AST
Aspartate Aminotransferase
BD
Becton Dickinson
BMI
Body Mass Index
BMI
SDS—Body Mass Index Standard Deviation Score
ELISA
Enzyme—Linked Immunosorbent Assay
GGT
Gamma—Glutamyl Transferase
HDL
High—Density Lipoprotein
HGB
Hemoglobin
HOMA
IR—Homeostatic Model Assessment of Insulin Resistance
IBM
International Business Machines
IL
4—Interleukin—4
IL
13—Interleukin—13
IR
Insulin Resistance
LDL
Low—Density Lipoprotein
METRNL / Metrnl
Meteorin—like Protein

PLT
Platelet Count
ROC
Receiver Operating Characteristic
rpm
Revolutions Per Minute
SD
Standard Deviation
SDS
Standard Deviation Score
SPSS
Statistical Package for the Social Sciences
TG
Triglyceride
TSH
Thyroid—Stimulating Hormone
T4
Thyroxine
UK
United Kingdom
USA
United States of America
WBC
White Blood Cell
WHO
World Health Organization

Declarations

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Consent for publication

Not applicable.

Availability of data and materials

Data and materials can be obtained by contacting the corresponding author.

Competing Interests

The authors declare no competing interests.

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Authors' contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript. IK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. HNPK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Writing – original draft, Writing – review & editing. SCD: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Writing – original draft, Writing – review & editing. MY: Conceptualization, Data curation, Formal analysis, Investigation, Methodology,

Data availability

Data can be obtained by contacting the corresponding author.

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Figures

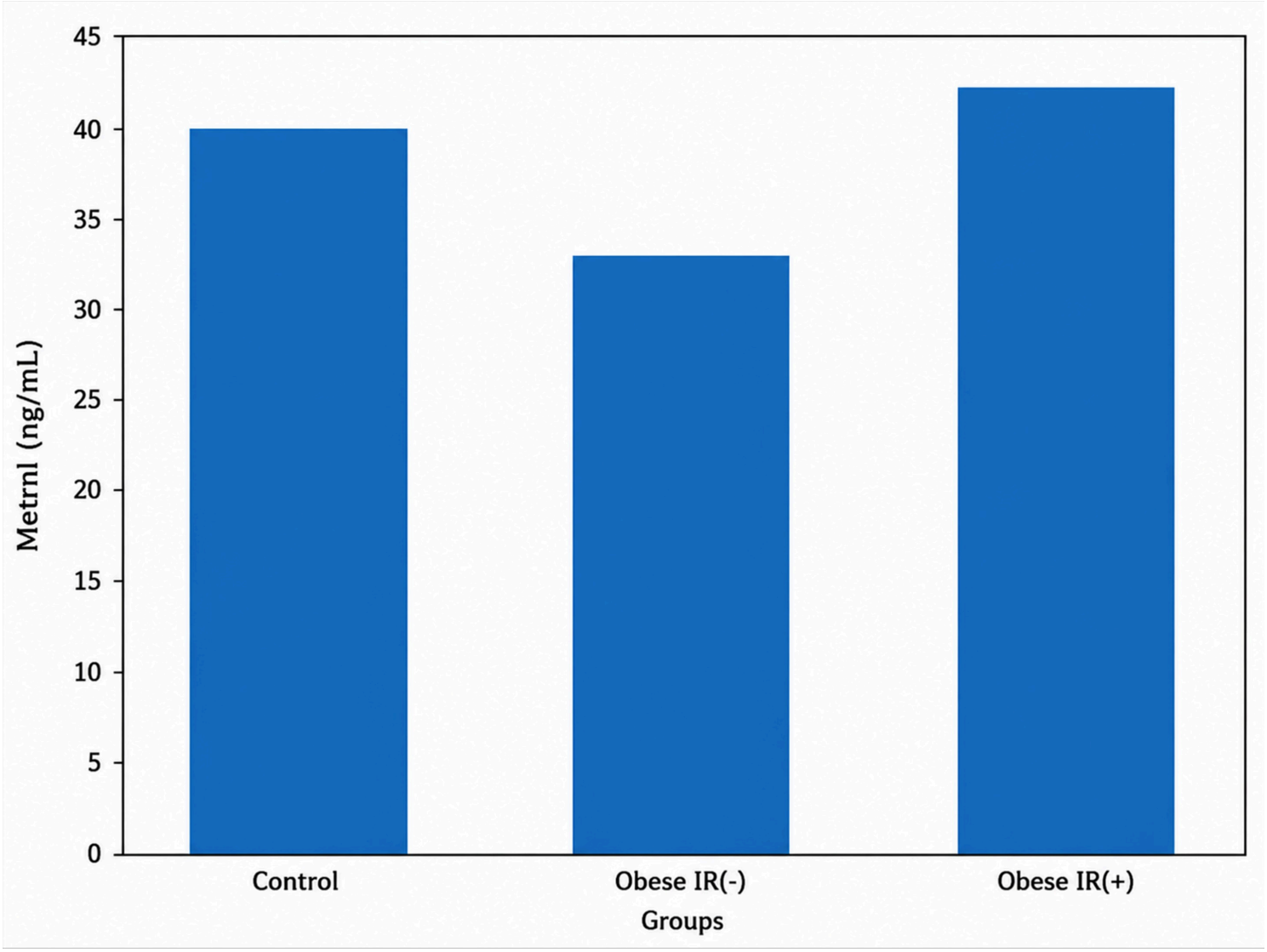

Figure 1

Serum Metrnl levels by group

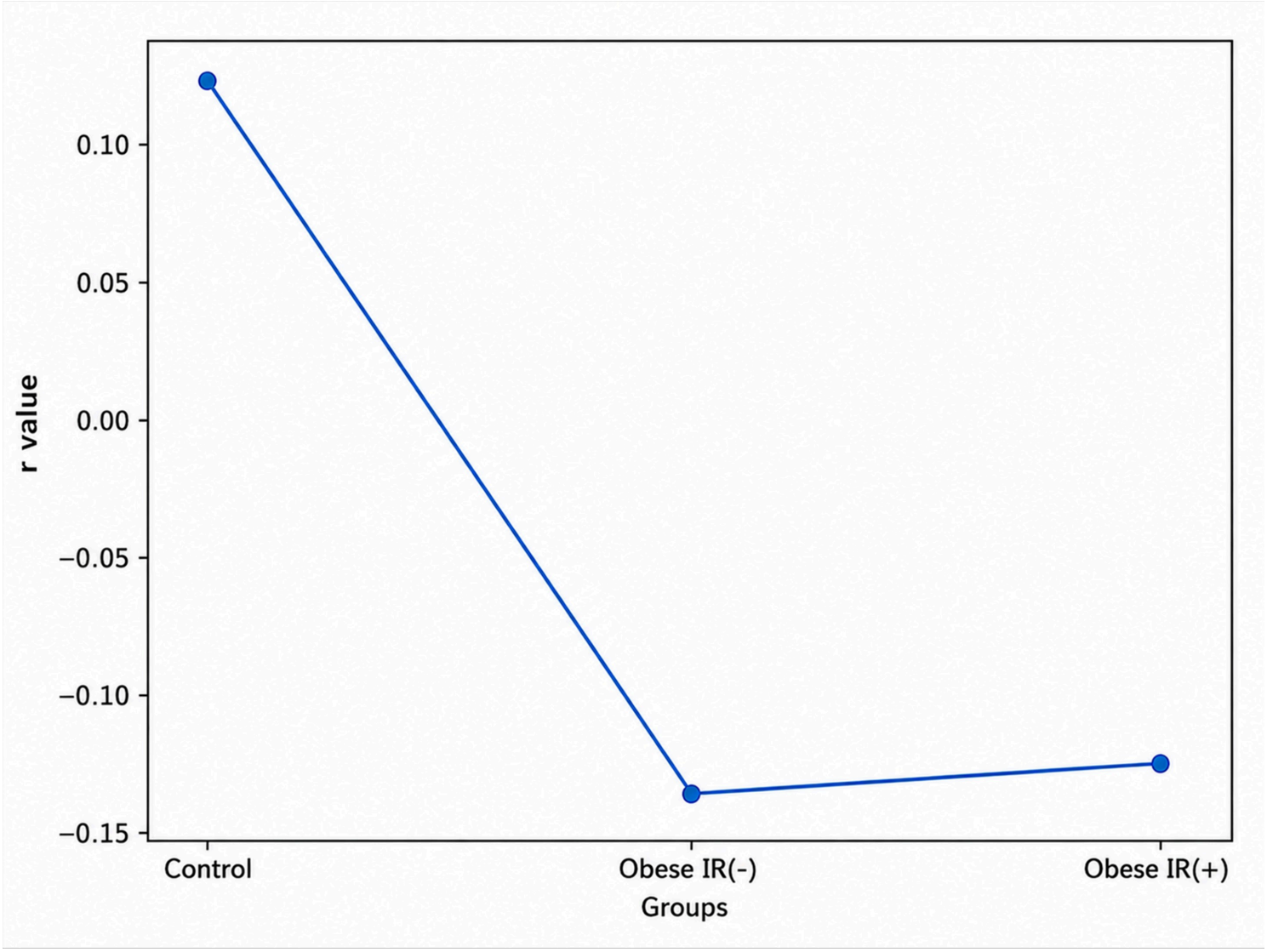

Figure 2

Metrnl–HOMA-IR Correlation

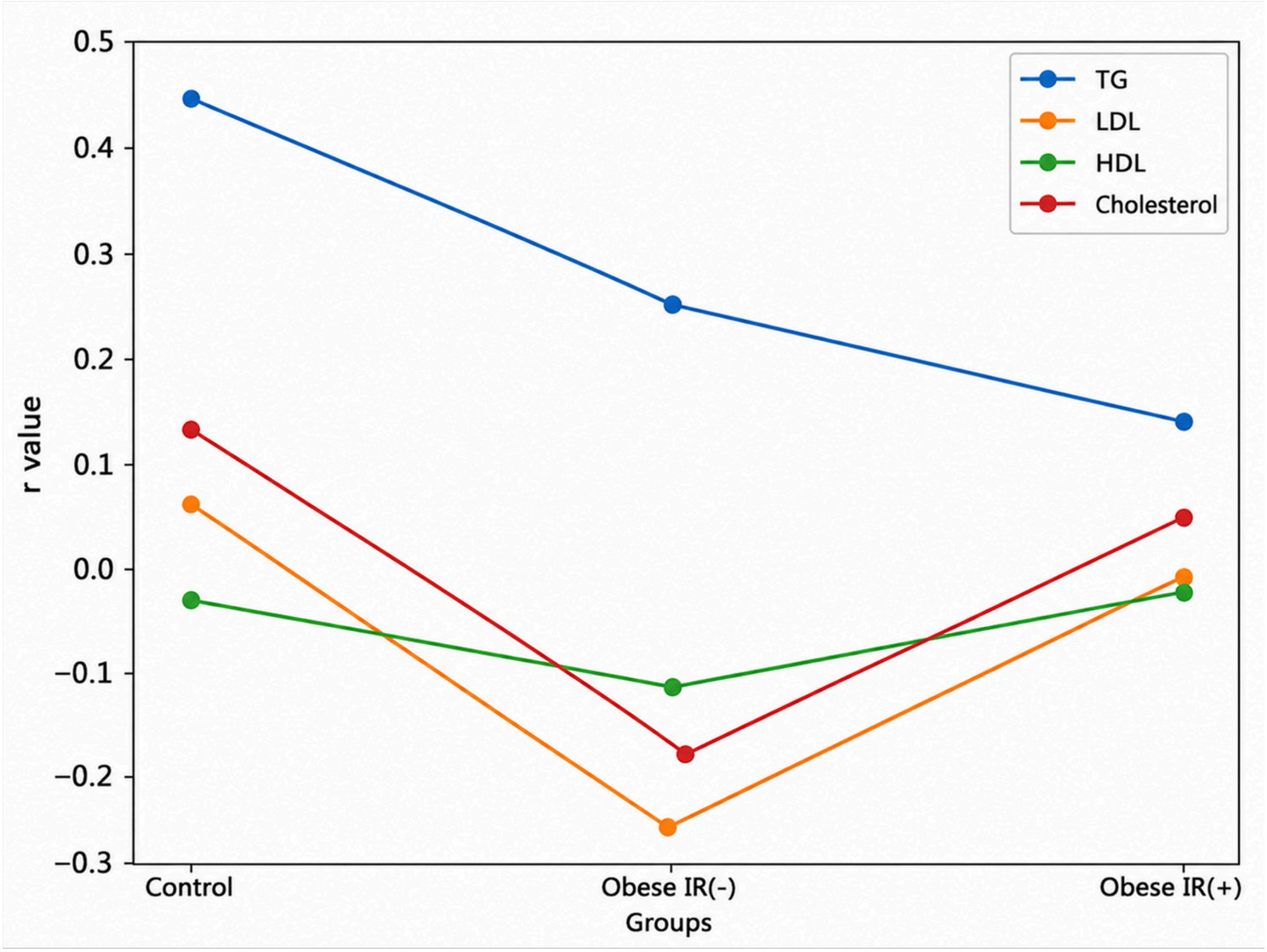

Figure 3

Metrnl–Lipid Correlations