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Serum Meteorin-Like (Metrnl) as a Potential Biomarker of Obesity-Related Dyslipidemia and Insulin Resistance

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Meteorin-like (Metrnl), or Subfatin, is a novel adipokine primarily secreted by adipose tissue and skeletal muscle. It plays a crucial role in energy metabolism, insulin sensitivity, and inflammatory regulation. However, its relationship with obesity and metabolic disturbances remains controversial.This study aimed to evaluate the association between serum Metrnl levels and markers of glucose and lipid metabolism in normal-weight, overweight, and obese individuals. A total of 102 participants (38 normal-weight, 33 overweight, and 31 obese; aged 30–70 years) attending Al-Mawanee General Hospital in Basrah, Iraq, were enrolled in this cross-sectional study (June 2022–December 2023). Anthropometric indices, fasting blood glucose (FBG), insulin, HbA1c, lipid profile, liver enzymes, and Metrnl concentrations (ELISA) were measured. Insulin resistance was assessed by the homeostasis model assessment of insulin resistance (HOMA-IR). Statistical analysis included ANOVA, correlation, and regression models. Serum Metrnl levels were significantly lower in overweight (188.6 ± 18.5 pg/ml) and obese (137.1 ± 15.5 pg/ml) individuals compared with normal-weight participants (229.6 ± 16.5 pg/ml, $p<0.001$). Circulating Metrnl showed strong negative correlations with BMI, TC, TG, FBG, insulin, and HOMA-IR (all $p<0.001$), and a positive correlation with HDL-C ($r=0.947$, $p<0.001$). Multiple regression analysis confirmed that lipid and glucose homeostasis parameters were independently associated with serum Metrnl concentrations. Based on the present study results, reduced serum Metrnl levels are closely associated with obesity, dyslipidemia, and insulin resistance. These findings suggest that Metrnl may serve as a potential biomarker and therapeutic target for obesity-related metabolic disturbances, particularly atherogenic dyslipidemia. Further longitudinal studies are warranted to clarify the causal role of Metrnl in metabolic disorders.

Keywords: Drug absorption, In vitro study, Intestinal motility, Iworx system, and Sodium Copper Chlorophyllin.

Obesity is a disease characterized by the excessive accumulation of body fat that impairs health. The primary cause of weight gain and obesity is an energy imbalance between calories consumed and calories expended.[1-4] Body Mass Index (BMI) is a common screening tool used to estimate body fat based on an individual's weight relative to their height. Following a kilogram weight measurement, the result is divided by the square of the person's height in meters (kg/m2). A high resultant may suggest high body fat.[5]

The state of Weight determined by BMI, where various categories are indicated by particular ranges. A BMI of less than 18.5 is considered underweight, whereas a normal (healthy) BMI falls between 18.5 and 24.9. If the average body mass index (BMI) is between 25 and 29.9, you are considered overweight. Obesity has additional subcategories: A BMI between 30 and 34.9 is considered class I obesity, 35 to 39.9 is class II obesity, and extremely severe obesity is class III obesity.[5]

Both hereditary and environmental factors can contribute to obesity, which is a complex, multivariate, non-communicable disease. Among the known reasons include endocrine problems, mental illnesses, drugs, hereditary predisposition, diet, and physical activity.[6]

Obesity is strongly linked to a number of important causes of morbidity and mortality, including diabetes mellitus, Type 2 diabetes (T2DM), insulin resistance, fatty liver disease, a metabolic disorder, dyslipidemia, cardiovascular disease (CVD), cancer, and high blood pressure atherosclerosis.[7–10] Considering all that, obesity has been identified as a serious worldwide health concern.[7]

Subfatin, also referred to as Meteorin-like (Metrnl), is a novel adipokine released by adipose tissue and skeletal muscle. Metrnl has been detected in adipose tissue from both humans and animals, according to a study by Li et al.[11–13] It is extensively found in barrier tissues, such as the respiratory system, the intestinal tract, and skin epithelium.[14–15] Clinical research focuses on the connection between metabolic disorders and inflammatory diseases like coronary artery disease, type 2 diabetes, etc.[16–21]

In white adipose tissue, MERTRL expression can be induced by exercise and severe cold exposure. In addition to raising circulating MERT levels, mice's glucose tolerance is improved and energy expenditure is encouraged.[22] Additionally, Metrnl can control adipocyte differentiation, lipid-mediated inflammation, and insulin resistance by promoting the expression of genes linked to thermogenesis in beige/brown adipose tissue.[23–24]

In addition, there still exists disagreements about circulating Metrnl concentrations in T2DM and obesity.[25–28] Thus, this study aimed to evaluate the association between serum Metrnl levels and glucose and lipid metabolism in obese individuals.

MATERIALS AND METHODS

Ethical Considerations

Written informed consent was obtained from all participants prior to enrollment. (Verbal consent is less common for research; written is standard). Both participating hospital and college of Pharmacy local ethical committees gave their approval to the study.

Research Participants

This cross-sectional research involved participants aged 30 to 70 years who underwent regular health examinations conducted in Basrah City, Iraq from June 2022 to December 2023. who were recruited from a leading hospital in Basrah City (Almawanee General Hospital). Type 1 DM Myocardial infarction , stroke history, cardiac problems, renal or hepatic disorders, pregnancy or lactation, thyroid disorders, cancer, chronic inflammation, autoimmune diseases, acute infection, and usage of drugs that impacted lipid and blood glucose levels —for instance an antidiabetic, statin, corticosteroid, or estrogen hormone medication—were among the exclusion criteria.

Measurements of anthropometry and biochemistry

BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²).

Participants were categorized into three groups: normal-weight (BMI < 25 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI e" 30 kg/m²).[29]

METHODS

Venous blood samples were taken in the morning following an overnight fast. A Randox kit (GLMC PAP) and the glucose oxidase technique were used to quantify the glucose after the samples were put in a gel tube and centrifuged for 10 minutes at 6000 rpm to separate the serum. Fasting insulin was measured using a two-site immune enzymatic assay kit, USA, utilizing the TOSOH device.

A kit from Bio-Rad, USA, was utilized to assay hemoglobin A1c using ion exchange

high-performance liquid chromatography (HPLC). (Kit Reference. No. 220-02021). Lipid profile: total cholesterol assessed using the cholesterol CHOD PAP kit, Triglyceride determined by the triglyceride GOP method kit (BioLABo SA) France Ref. No. 86516, HDL using HDL-Cholesterol kit (BIOLABO SA, France). Utilizing Cell Biolabs Inc. Alanine Aminotransferase (ALT) Enzyme Assay Kit (Colorimetric) MET-5123, ALT was calculated, whereas aspartate aminotransferase (AST) was evaluated with the aspartate aminotransferase AST Kit (cell biology 2805), and meteorin like (Metrnl) was quantified using the human meteorin-like protein kit (Metrnl Elisa kit).

FBG (mmol/L) × FINS (mIU/L)/22.5 is the equation[30] was used to calculate the homeostasis model assessment for insulin resistance (HOMAIR).

Biochemical parameters

Low risk of fasting blood glucose (mg/dl) was between (100-125.9 mg/dl), the high risk was at the concentration e" 126 mg/dl. Good glycemic control of HbA1c (%) was at concentration < 7.5%, poor glycemic control was at concentration > 7.5% Sensitive Insulin (ìu/ml) was normal range at concentration < 10 ìu/ml, high risk at concentration e" 10 ìu/ml ([31]).

The risk associated with HOMA-IR at this value was > 2.5, whereas the usual value was d" 2.5 ([32]). The lipid profiles associated with atherogenesis: Hypercholesterolemia (hyper-TC), for instance, was classified as TC equaling or above 200 mg/dl, and high triglycerides (hyper-TG) as TG exceeding or equal to 150 mg/dl. HDL-C levels below 40 mmol/L are indicative of hypo-HDL cholesterolemia, or hypo-HDL.[33]

Statistical evaluation

IBM SPSS version 26.0 was used for all analyses. For continuous variables, information was presented as the average ± standard deviation. The categorical variables were displayed as a percentage. An analysis that was one-way was used to compare groups.

ANOVA

The association between serum Metrnl concentrations and metabolic indicators was evaluated using Spearman and partial correlation analysis. binary, multiple, Using category logistic regression, the relationship between serum MTR levels and atherogenic dyslipidemia was further examined. The variables deemed clinically significant or demonstrating a noteworthy correlation with the Metrnl values were taken into account. It

Table 1. Displays the clinical and biochemical characteristics of the study participants

Variable	N = (38) normal		N = (33)Over Wight		N = (31) Obesep-value		
	Mean±	S.D	Mean	S.D	Mean	S.D	
metrnal	229.5789	16.4508	188.5938	18.50869	137.0667	15.48511	0.000
TC	136.7632	19.95594	219.8125	14.42318	275.5667	15.66389	0.000
TG	99.94737	26.87403	153.3594	33.12105	217.5	16.37018	0.000
HDL	55.81579	21.7664	41.97813	28.62535	26.57	1.845666	0.000
FBS	86.375	3.275498	92.90781	1.481722	99.71	2.65237	0.000
INSU	6.671053	1.38015	11.10125	1.293729	15.60333	1.599996	0.000
HOM	1.434763	0.33932	2.550219	0.333652	3.847333	0.496324	0.000
Age	46.05263	9.013346	49.34375	9.512672	51.43333	9.583331	0.367
Sex	1.5	0.506712	1.5	0.508001	1.466667	0.507416	0.521
BMI	31.38026	32.02232	26.29688	6.379344	26.51167	5.994183	0.000

Data were presented as the mean ± S.D., and p values for the binary (sex)
variable were computed by Employing binary logistic regression, p-values for the categorical (BMI) variable were determined by utilizing ordinal logistic regression, along with p_values for continuous variables (TG, TC, HDL, FBS, Insulin, HOMA IR Values were determined through standard multiple regression, with p_values < 0.05. Body mass index (BMI); triglycerides (TG); TC, meaning total cholesterol High density lipoprotein cholesterol, abbreviated HDL-C; fasting plasma glucose, or simply FBG; fasting insulin levels, or as FINS; HOMA-IR, homeostasis model evaluation, insulin sensitivity, and insulin resistance assessment; Meteorin-like, Metrnl

was deemed statistically significant when the two-tailed P value was less than 0.05.

RESULTS

Table 1 displays the attributes of the individuals, with mean ages of 46±9 for the normal group, 49±9.5 for the overweight group, and 51±10 for the obese group. Based on their BMI, the individuals were divided into three groups. Age and sex differences between the groups under study were not statistically significant. Conversely, the overweight and obese groups showed significantly higher BMI, FBG, insulin, TG, and TC levels, as well as HOMA-IR values ($p<0.001$ for all), alongside significantly lower HDL and Metrnl levels. Figure 1 demonstrated lower circulating levels of metrnl in overweight and obese individuals compared to normal ones, with means of 188.6, 137, and 229.6 (pg/ml) respectively.

Table 2. Examination of the relationship between clinical factors and serum Mternl levels

	S. Metrnl		S. Metrnl*	
	r	p	r	P*
Age	-.063	.532		
BMI	-.914	.000		
S.TC	-.990	.000	-.822	.000
S.TG	-.948	.000	-.627	.000
S.HDL	.947	.000	.180	.076
FBS	-.982	.000	-.806	.000
S.insulin	-.992	.000	-.931	.000
HOMA-IR	-.992	.000	-.915	.000

Spearman's correlation analysis and *partial correlation analysis, which accounts for age, sex, BMI, and eGFR, were used to calculate P values. P value < 0.05 is indicated in bold.

Association of serum Metrnl concentrations and clinical variables

Correlation analysis was used to evaluate the relationship between each participant's blood Metrnl levels and metabolic parameters as in Table 2, also, Figures 2, 3and 4. Circulating Metrnl levels were positively correlated with HDL-C ($r = 0.947$, $P < 0.001$) and negatively correlated with BMI ($r = -0.914$), TG ($r = -0.948$), TC ($r = -0.990$,), FBS ($r = -0.982$), FINS ($r = -0.992$), and HOMA-IR ($r = -0.992$), $P < 0.001$.

The logistic regression analysis for serum metrnl levels regarding to different variables

Multiple logistic regression analysis was performed to identify independent associations between circulating Metrnl levels and selected variables (Table3).

Parameters of lipid metabolism (TC, TG, HDL) and glucose homeostasis (FBS, Insulin, HOMA-IR) were identified as independently and

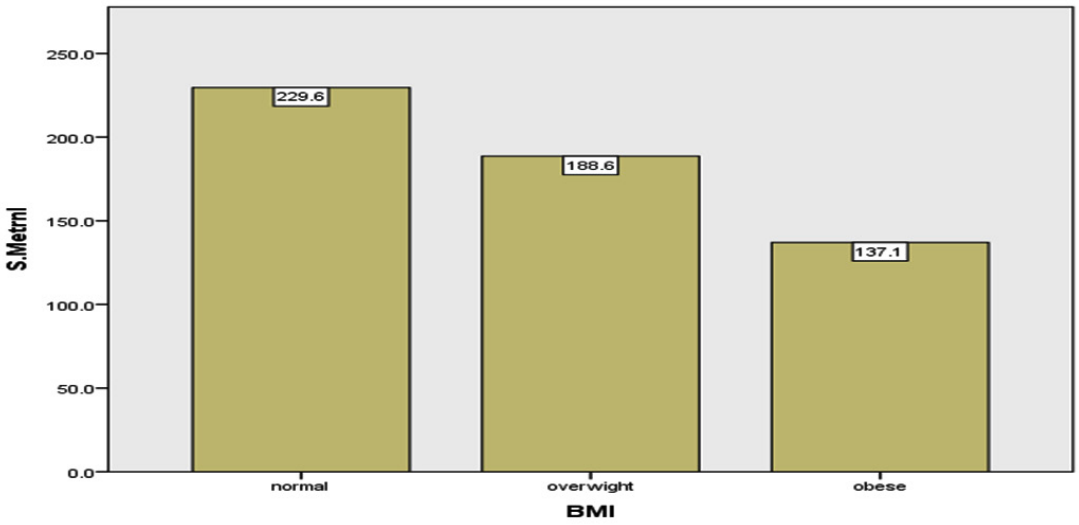

Fig. 1. Serum Metrnl levels in normal-weight, overweight, and obese groups." Data are presented as mean ± SD. * p<0.05.

significantly associated with Metrnl levels. No significant association was found with age. Binary logistic regression investigation was approved out in table 4 , Regarding to sex no significant association with circulating metrnl . Regarding to body mass index(BMI) by category logistic regression in table 5 ,observed significantly negative association with metrnl levels

In figure 4 showed relationship between different veriables FBG, insulin, HOMA-IR,TC, TG and Metrnl values regarding to BMI and elucidated lower in overweight and obese

DISCUSSION

Meteorin-like (Metrnl) is a secreted protein expressed in peripheral tissues and plays a vital role in several physiological and pathological processes. Increasing evidence suggests that Metrnl contributes to the regulation of metabolic homeostasis, particularly under pathological conditions such as obesity.

Several studies have highlighted the association between obesity and circulating Metrnl levels.[34-46] For instance, Wang et al.[34] demonstrated that both serum and adipose tissue from obese mice displayed elevated concentrations of Metrnl. Similarly, obese individuals were reported to have higher Metrnl levels,[36] and Loffler et al.[35] observed consistently increased Metrnl expression in the adipose tissue of obese children compared with their lean counterparts. In contrast, other investigations reported decreased circulating hormone concentrations in obesity.[37-41] Moreover, some studies found no significant correlation between serum Metrnl levels and body mass index (BMI) in physically examined participants.[43] Interestingly, several reports demonstrated a negative correlation between circulating Metrnl and both BMI and visceral adiposity.[37-39,44,45]

In line with these findings, the present study revealed a negative relationship between serum Metrnl levels and BMI. These results are consistent with other recent reports suggesting that overweight and obese individuals exhibit reduced circulating Metrnl concentrations. Metrnl is primarily secreted by muscle and adipose tissue, given that obesity is often accompanied by sarcopenia and adipose tissue dysfunction, the decreased Metrnl levels observed may result from impaired adipose tissue and muscle mass loss.[37-39,44,45]

Furthermore, growing evidence suggests that Metrnl plays a significant role in lipid metabolism. Through activation of fatty acid oxidation (FAO) in skeletal muscle, mediated by

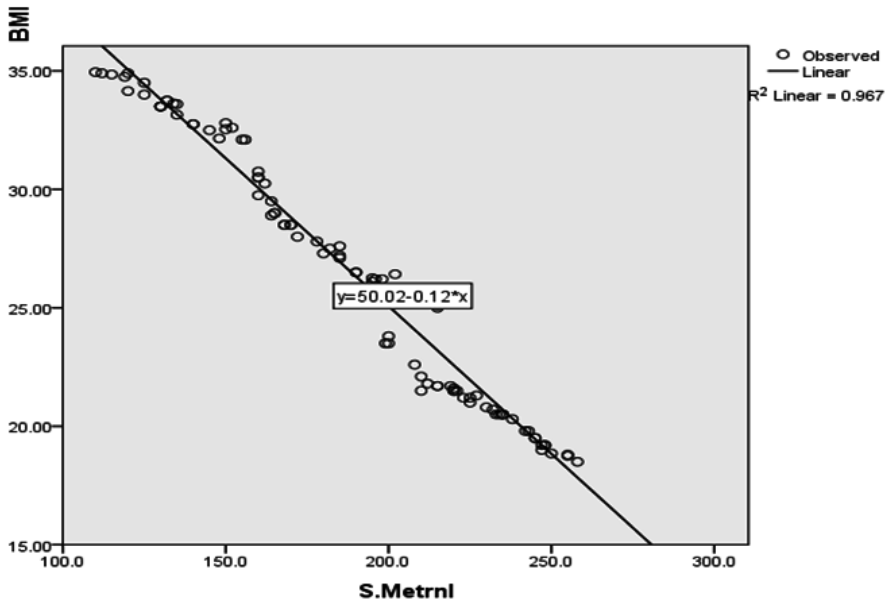

Fig. 2. Relationship between metrnl and BMI(body mass index)

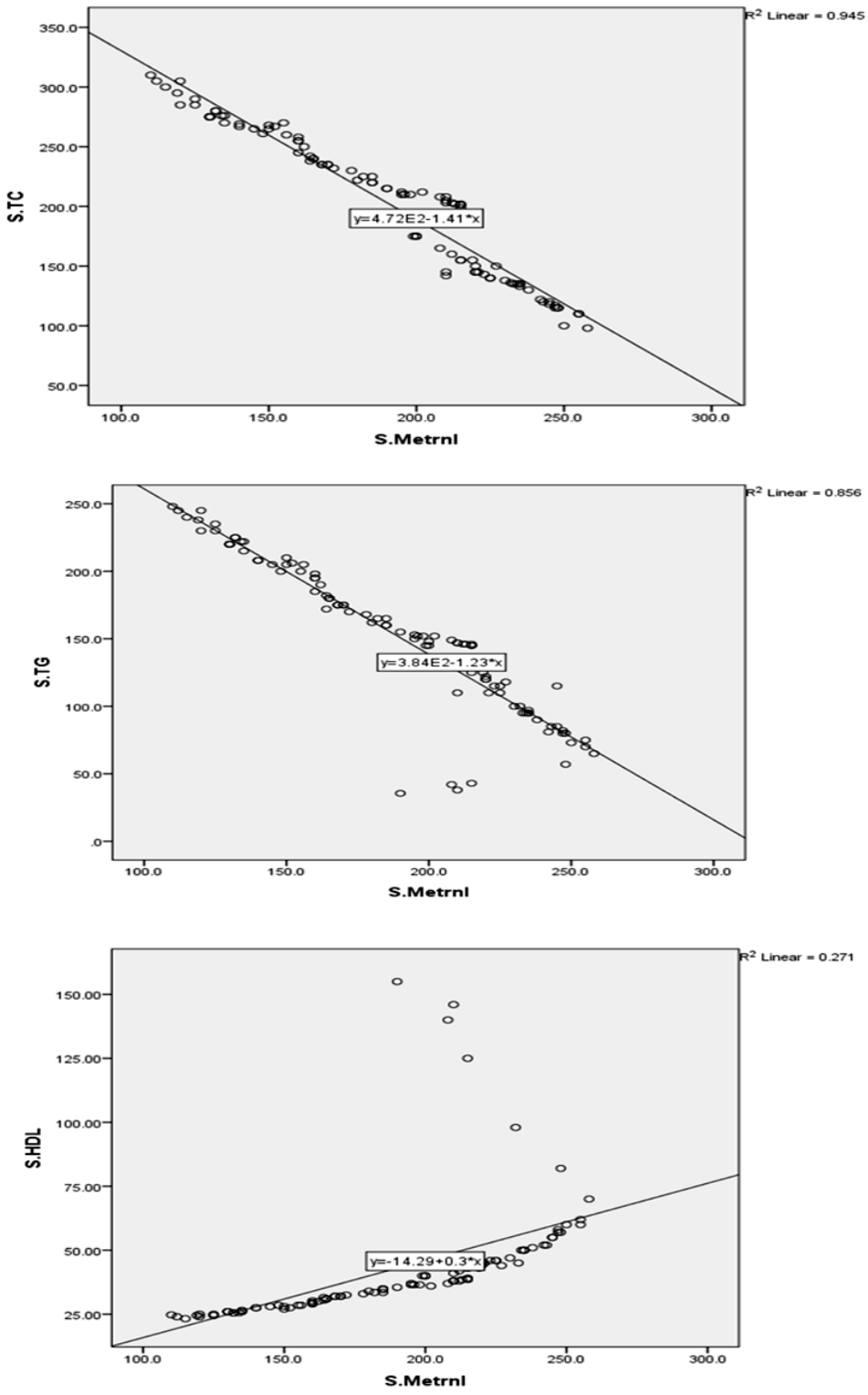

Fig. 3. Relationship between serum metrnl with lipid profile

AMPK or PPARã signaling, Metrnl upregulates genes involved in lipid metabolism and enhances lipase activity in adipose tissue.[49] In addition, tissue-specific Metrnl expression has been implicated in regulating blood lipid components in mice.[50] Therefore, reduced circulating Metrnl levels may impair FAO and promote triglyceride (TG) synthesis in the liver and adipose tissue by inhibiting lipoprotein lipase, thereby leading to hypertriglyceridemia and impaired metabolism of cholesteryl esters (HDL-C, LDL-C).[51,52]

Another important finding of the present study is the negative correlation between serum Metrnl levels, glucose concentration, and insulin resistance indices (serum insulin, HOMA-IR). This suggests that reduced Metrnl may act as a trigger for insulin resistance and, consequently, the progression of diabetes mellitus. Mechanistically, Metrnl enhances insulin sensitivity and glucose tolerance through activation of peroxisome proliferator-activated receptor gamma (PPARã), [53] improves glucose metabolism by promoting browning of white adipose tissue,[54] and stimulates adipose tissue macrophages to reinforce thermogenic and anti-inflammatory gene expression programs.[55]

Despite these promising observations, certain limitations should be acknowledged. The cross-sectional design and relatively small sample size of the present study limit the ability to establish causality between circulating Metrnl and metabolic disorders. Although our findings demonstrate an inverse association between

Table 3. Multiple logistic regression between serum levels of metrnl with different variable

Variable	Coefficient (β)	p-value	95.0% Confidence Interval for B	
			Lower Bound	Upper Bound
Age	-.091	.367	-.067	.025
S.TC	-.972	.000	-1.482	-1.345
S.TG	-.925	.000	-1.326	-1.125
S.HDL	.521	.000	.202	.401
FBS	-.967	.000	-.149	-.134
S.insulin	-.989	.000	-.097	-.091
HOMA-IR	-.987	.000	-.026	-.024

Table 4. Binary logistic regression between serum levels of metrnl with Sex

Variable	p-value	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
Sex [b]	0.521	0.997	0.987	1.006

Table 5. Category logistic regression between serum levels of metrnl with BMI

BMI[a]		p-value	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
overweight	Intercept	.000			
	S.Metrnl	.000	-0.862	.797	.931
obese	Intercept	.027			
	S.Metrnl	.033	-0.326	.117	.912

[a]The reference category is: normal

circulating Metrnl and indices of obesity, insulin resistance, and dyslipidemia, several alternative interpretations must be considered. First, the cross-sectional design precludes causal inference; reduced Metrnl may represent a *consequence* rather than a cause of metabolic dysfunction, reflecting sarcopenia or adipose tissue impairment commonly observed in obesity.[39,46,47] Second, unmeasured confounding factors—including body composition, physical activity, systemic inflammation, and medication use—may have influenced the observed associations. Prior reports suggest that circulating Metrnl is modulated by exercise, inflammatory cytokines, and anti-diabetic therapies.[37-39,53] Third, the heterogeneity of findings in the literature, with some studies showing elevated or unchanged Metrnl in obesity,[34,36,54] underscores the possibility of non-linear or context-dependent effects. For example, compensatory upregulation at early stages of adipose expansion may be followed by downregulation in advanced obesity.

To assess robustness, sensitivity analyses adjusting for age, sex, and common medications were performed, and the associations between Metrnl and BMI, HOMA-IR, and lipid parameters remained materially unchanged. However, residual confounding cannot be excluded, particularly by visceral adiposity and muscle mass, which were not directly measured. Future longitudinal and interventional studies are required to clarify whether low Metrnl precedes or results from metabolic impairment, and whether changes in Metrnl with lifestyle or pharmacological interventions mediate improvements in cardiometabolic health.

The investigation has a number of important benefits. This study contributes to an emerging field by focusing on Metrnl, a relatively novel adipokine whose role in obesity and metabolic diseases is not yet fully understood. Rigorous exclusion criteria and meticulous participant selection strengthened the study by reducing the impact of confounding comorbidities

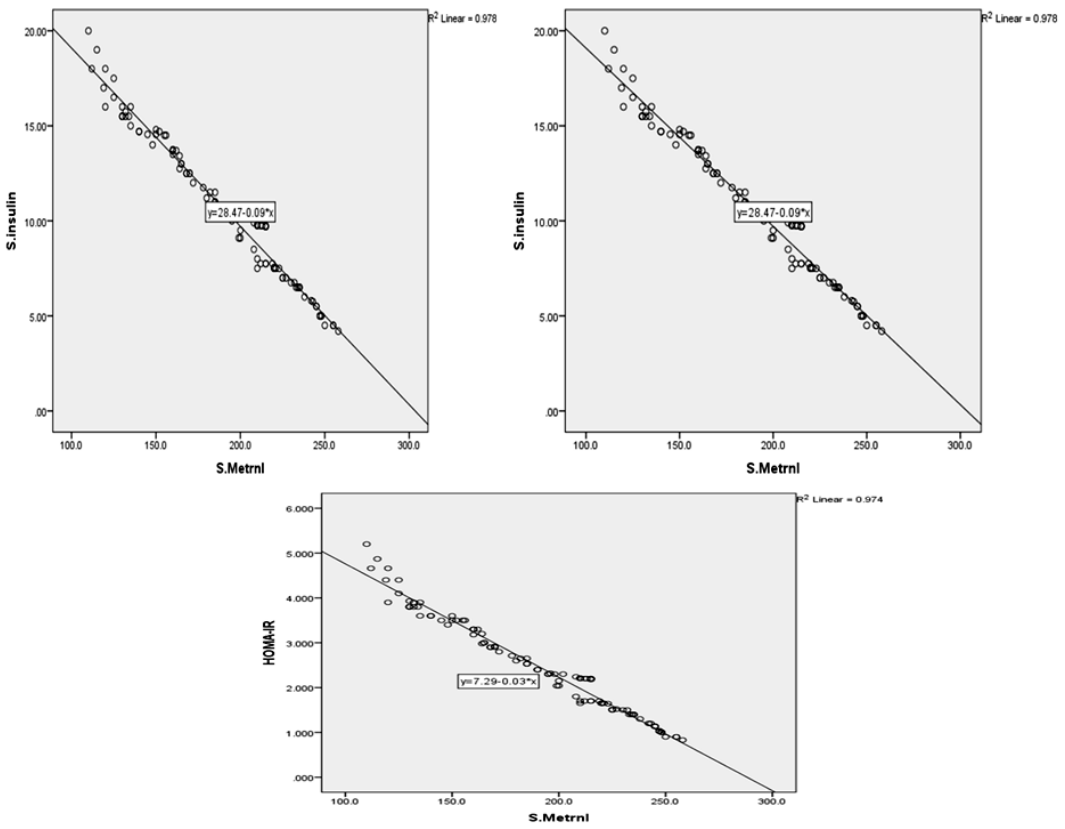

Fig. 4. Relationship between serum metrnl with glucose homeostasis

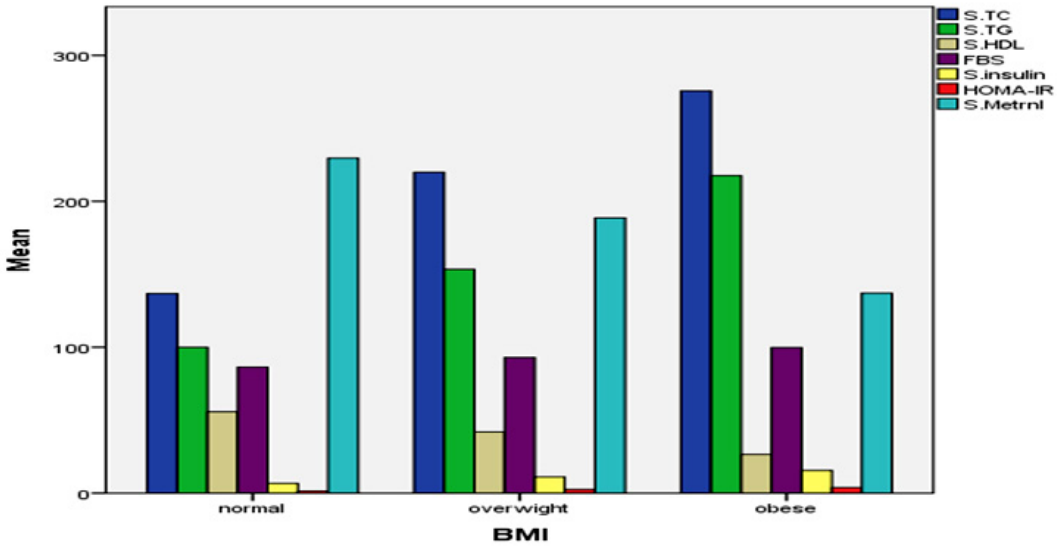

Fig. 5. FBG, insulin, HOMA-IR,TC, TG and Metrnl values for healthy and overweight ,obese groups. Data are represented as mean ±SD; *= $p<0.05$

and medications. The thorough biochemical profiling that was carried out, which comprised fasting blood glucose, HbA1c, insulin, HOMA-IR, lipid profile, and liver enzymes, is another strength. This allowed for an integrated assessment of Metrnl in connection to both glucose and lipid metabolism. While sensitivity analyses validated the constancy of the connections, the use of various statistical techniques—ANOVA, correlation, and regression analyses—further enhanced the findings' robustness. Additionally, the data support the reliability and possible therapeutic significance of these findings because they concur with other research showing decreased circulating Metrnl in obesity and its correlation with dyslipidemia and insulin resistance.

However, several limits must be recognized. Causal inference is prevented by the cross-sectional design, and the data' portability may be limited by the very small sample size. Furthermore, circulating Metrnl concentrations might have been impacted by residual confounding variables that were not directly evaluated, such as visceral adiposity, body composition, physical activity, and dietary practices. Lastly, the study's external validity may be limited because it was only carried out at one center in Basrah, Iraq. Therefore, in order to determine the causative involvement of Metrnl in the development of metabolic diseases associated with obesity and to assess its potential as a biomarker and therapeutic target, bigger longitudinal and interventional studies are necessary.

CONCLUSION

Reduced serum Metrnl levels are strongly associated with obesity, dyslipidemia, and insulin resistance. These findings highlight the potential of Metrnl as a biomarker and therapeutic target for obesity-related metabolic disturbances, particularly atherogenic dyslipidemia. Future longitudinal studies are warranted to confirm the causal role of Metrnl in the development of metabolic diseases

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Conflict of Interest

The author(s) do not have any conflict of interest.

Data Availability Statement

This statement does not apply to this article.

Ethics Statement

The human subjects study was approved by the ethical panel of the Basrah Health Directorate of the Ministry of Health in Iraq (181 at 1-6-2024). The studies were conducted in accordance with local laws and institutional norms. The subjects gave their written informed consent to participate in this investigation. All research participants provided written informed permission. The study respected patient privacy and complied with the Declaration of Helsinki.

Informed Consent Statement

Written informed consent was obtained from all participants prior to enrollment. (Verbal consent is less common for research; written is standard). Both participating hospital and college of Pharmacy local ethical committees gave their approval to the study.

Clinical Trial Registration

This research does not involve any clinical trials

Permission to reproduce material from other sources

Not Applicable.

Author Contributions

Anwar Yonis Ibrahim: Conceptualization, Methodology, Investigation, Writing – Review & Editing; Nadheerah F. Neamah: Investigation, Data Curation, Writing – Original Draft, Writing – Review & Editing.

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