The Egyptian Journal of Hospital Medicine (April 2023) Vol. 91, Page 4333-4339

Evaluation of Circulating Serum Meteorin-like Protein Levels in Obesity and Type 2 Diabetes Mellitus

Islam Maher Wahid [1], Amira Shoukry Ahmed Soliman [1], Naday Faez Yousuf*[1], Ahmed Abdulsaboor Mohammed[2]

[1]Department of Internal Medicine and Department of Clinical Pathology, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Naday Faez Yousuf, **Mobile:** (+20) 01284990809, **E-mail: Yousefaljabery99@gmail.com**

ABSTRACT

Background: Given the burden that diabetes and obesity place on patients' quality of life and healthcare systems, elucidating the relationships between diabetes, insulin resistance, and meteorin-like protein may be useful in improving understanding of the pathological processes underlying those clinical conditions. Therefore, this study aimed to evaluate the circulating serum meteorin-like protein levels in patients with obesity and type 2 diabetes mellitus (T2DM) in an attempt to elucidate possible relationships between serum meteorin levels with anthropometric and metabolic parameters of T2DM and obesity.

Subjects and methods: The study was cross-sectional case-control observational study, carried out in outpatient clinic of Internal Medicine Department, Endocrinology and Metabolism Unit, and Department of Clinical Pathology, Faculty of Medicine, Zagazig University Hospitals from August 2022 to February 2023. This study was carried out on 104 subjects divided into two groups: non-diabetic subjects group and newly diagnosed type 2 diabetic patient group, with futher subdivision according to BMI to obese and non obese subgroup.

Results: Serum meteorin-like protein levels in newly diagnosed T2DM patients were statistically substantially higher than in nondiabetic controls. Furthermore, when these groups were separated into nonobese and obese subgroups, we discovered that serum meteorin levels were considerably greater in obese nondiabetic controls and obese diabetic patients, than in nonobese nondiabetic controls and nonobese diabetic patients, respectively. Obese T2DM patients had the highest serum meteorin levels.

Conclusion: Circulating serum meteorin-like protein levels were increased in newly diagnosed T2DM and obesity.

Keywords: Meteorin-like protein, Type 2 Diabetes Mellitus, Obesity.

INTRODUCTION

Impairment of insulin production and varying levels of peripheral insulin resistance (IR) are symptoms of diabetes mellitus (DM), which results in hyperglycemia [(1)]. It is classified as a lipid, protein, and carbohydrate metabolic disease. The frequency of DM has significantly increased in recent years, posing a serious hazard to public health [(2)].

Type 2 diabetes affects more than 90% of persons with the condition. The disease is very common among ethnic groups and in family members of those who have the condition are both indications that there are obvious genetic drivers. Although a number of genetic variants have been discovered during the past several years, the most prevalent forms of T2DM are not caused by a single gene [(3)].

In the world, type 2 diabetes mellitus (T2DM) is one of the most common co-morbidities, and its incidence is rapidly rising. The most prevalent kind of hyperglycemia, insulin resistance, and a relative shortage of insulin are signs of diabetes [(4)].

Additionally, the epidemic of obesity worldwide is responsible for the concurrently rising prevalence of cardiometabolic illnesses, such as T2DM [(5)]. It is commonly known that insulin resistance (IR), obesity, and prediabetes are all closely related [(6)].

T2DM development is at risk due to insulin resistance (IR). As novel insulin-sensitizing medications are required, improving IR is still a crucial field of study for the treatment of T2DM and metabolic syndrome [(7)].

Adipokines and myokines are examples of secreted proteins that have been demonstrated to be strongly related to the emergence of IR and may one day be used as therapeutic targets for the treatment of T2DM and obesity [(8,9)].

The purpose of this study was to look at circulating serum meteorin-like protein levels in individuals with obesity and type 2 diabetes mellitus (T2DM) to see if there were any links between serum meteorin levels and anthropometric and metabolic parameters associated with T2DM and obesity.

PATIENTS AND METHODS

The study was cross-sectional case-control observational study, carried out in outpatient clinic of Internal Medicine Department Endocrinology and Metabolism Unit, and Department of Clinical Pathology, Faculty of Medicine, Zagazig University Hospitals from August 2022 to February 2023**.**

Received: 13/11/2022
Accepted: 15/01/2023

Inclusion criteria: Both control subjects and T2DM patients were within the age of 40 to 60 years old. Both genders were involved in the study. Patients with T2DM were newly diagnosed before treatment interventions. Both control subjects and T2DM patients group included obese and non-obese subjects.

Exclusion criteria: Age < 40 and > 60 years old. Patients with previously diagnosed T2DM on treatment, other forms of diabetes, and pharmaceutical history were not allowed to take anti-diabetics, statins, diuretics, corticosteroids, estrogen, or progestin, all of which impair glucose tolerance and insulin sensitivity.

This study was carried out on 104 subjects divided into two groups namely: non-diabetic control subjects group and type 2 diabetic patient group:

- **Group I (Non-diabetic subjects group)** this group includes 52 non diabetic subjects. They were divided according to their BMI into two sub-groups; **Group IA (non-diabetic non-obese control subjects):** this group included 26 subjects with BMI < 30 kg/m^2. **Group IB (Non-diabetic obese subjects):** this group included 26 subjects with BMI ≥ 30 kg/m^2.
- **Group II (T2DM patient group)** this group included 52 patients with newly diagnosed T2DM. The patients were divided according to their BMI into two sub-groups: **Group IIA (Non-obese T2DM patients)** this group included 26 T2DM patients with BMI < 30 kg/m^2. **Group IIB (Obese T2DM patients)** this group included 26 T2DM patients with BMI ≥ 30 kg/m^2.

Methods:

Every patient underwent a thorough clinical examination and detailed history taking were done for all patients including skin lesions (insulin resistance) and ulcers, peripheral pulsation, warmth, and skin color. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after more than five minutes of rest. Measurements taken for anthropometry were height, weight, and body mass index, waist circumference (WC), hip circumference (HC) and waist to hip ratio WHR. Each subject received a 75 g oral glucose tolerance test (OGTT) as part of laboratory studies, and postprandial blood glucose (PBG) was then measured. Bolus insulin, glycated blood hemoglobin (HbA1c), and renal function (urea and creatinine) were also estimated.

By multiplying the fasting insulin concentration, the homeostatic model assessment of insulin resistance (HOMA-IR) index was calculated (U/mL) by the fasting blood sugar (FBG) concentration (mg/dL). The concentrations of serum meteorin-like protein (MTN) were measured by enzyme-linked immunosorbent assay (ELISA) kits.

Ethics approval:

An informed written consent was obtained from all the participants. The study procedure was approved by Zagazig University's Institutional Review Board (IRB # 9716) and was carried out in accordance with the Helsinki Declaration principles.

Statistical Analysis

Data analysis was done using SPSS (Statistical Package for the Social Sciences) version 26. The absolute frequencies of the categorical variables were used to describe them, and the chi square test was used to compare them. The assumptions underlying parametric testing were examined using the Shapiro-Wilk test. Quantitative data were presented as the means and standard deviations. Utilizing Mann Whitney and independent sample t tests (for normally distributed data), quantitative data were compared between two groups. Spearman rank correlation coefficients were used to determine the strength and direction of the relationship between two continuous variables. The dependent factor's associated independent components were quantified using linear regression analysis. In order to evaluate statistical significance, a P 0.05 criterion was utilized. There was found to be a highly significant difference when the value of P 0.001 was used.

RESULTS

Table 1 indicates that diabetic patients' age, systolic, and diastolic blood pressure were significantly higher than non-diabetic controls. Considering the following factors; waist size, waist to hip ratio, body mass index, and gender, diabetic patients and non-diabetics did not differ statistically significantly from each other. When compared to non-diabetic people, diabetic patients had significantly higher levels of HbA1c, fasting insulin, postprandial blood sugar two hours later, fasting blood glucose, HOMA-IR, and serum meteorin-like protein. While there was no statistically significant difference in serum urea and creatinine levels between diabetic patients and non-diabetic subjects.

Table (1): Comparison between non-diabetic subjects and diabetic patient groups regarding demographic and clinical data

	Non-diabetic group	Diabetic group	χ^2	P
	N=52(%)	N=52(%)		
Gender: **Female** **Male**	 26 (50%) 26 (50%)	 31 (59.6%) 21 (40.4%)	0.971	0.325
	Mean ± SD	**Mean ± SD**	**T**	**P**
Age (year)	46.48 ± 11.58	51.52 ± 12.32	-2.149	**0.034***
Height (cm)	168.52 ± 7.79	165.29 ± 6.63	2.278	**0.025***
Weight (kg)	80.69 ± 13.06	80.1 ± 13.97	0.225	0.823
BMI (kg/m^2)	28.63 ± 4.84	29.16 ± 5.06	-0.551	0.583
WC (cm)	91.44 ± 20.17	94.17 ± 13.83	-0.806	0.422
WHR	0.84 ± 0.15	0.87 ± 0.15	-1.028	0.306
Systolic blood pressure (mmHg)	125.5 ± 19.71	141.85 ± 15.73	**-4.675**	**<0.001****
Diastolic blood pressure (mmHg)	70.29 ± 9.97	80.96 ± 10.67	**-12.307**	**<0.001****
Laboratory data				
Serum urea (mg/dl)	40.37 ± 8.11	42.88 ± 7.92	-1.602	0.112
Serum creatinine (mg/dl)	0.78 ± 0.13	0.8 ± 0.14	-0.439	0.662
HbA1c (%)	5.22 ± 0.5	8.36 ± 1.26	-16.742	**<0.001****
Fasting blood glucose (mg/dl)	94.4 ± 3.56	156.19 ± 28.27	-15.638	**<0.001****
2 hours postprandial blood glucose (mg/dl)	127.23 ± 10.7	223.88 ± 19.34	-31.535	**<0.001****
Fasting insulin (µU/mL)	11.46 ± 4.19	17.65 ± 3.5	**-6.457**	<0.001**
HOMA-IR	2.65 ± 0.13	7.2 ± 1.48	-12.213	**<0.001****
Meteorin-like protein(ng/ml)	3.73 ± 0.34	6.71 ± 1.4	**-7.808**	**<0.001****

χ^2Chi square test, t independent sample t test, *: Significant, **: Highly significant
HbA1c: glycated hemoglobin, HOMA-IR: homeostatic model assessment -insulin resistance, BMI: body mass index, WC: waist circumflex, WHR: waist to hip ratio.

Table 2 shows that there was a statistically significant rise in weight, body mass index, waist circumference, waist to hip ratio, systolic and diastolic blood pressure when obese non-diabetic participants were compared to non-obesity non-diabetic patients. Age differences between non-obese and obese non-diabetic participants were not statistically different.

Obese non-diabetic patients showed significantly greater levels of HbA1c, 2 hours postprandial blood glucose, fasting insulin, HOMA-IR, and serum meteorin-like protein when compared to non-obesity non-diabetic patients. There was no statistically significant distinction between non-obese and obese non-diabetic subjects regarding fasting blood glucose, serum urea and creatinine as shown table 2.

Table (2): Comparison between non-obese non-diabetic and obese non-diabetic subject groups regarding demographic and clinical data

	Non-obese non-diabetic group N=26(%)	Obese non-diabetic group N=26(%)	χ^2	P
Gender: Female Male	9 (34.6%) 17 (65.4%)	17 (65.4%) 9 (34.6%)	4.923	**0.027***
	Mean ± SD	**Mean ± SD**	**T**	**P**
Age (year)	47.88 ± 12.57	45.08 ± 10.56	0.872	0.387
Height (cm)	171.77 ± 8.12	165.27 ± 5.99	3.286	**0.002***
Weight (kg)	69.81 ± 6.32	91.58 ± 7.83	-11.029	**<0.001****
BMI (kg/m^2)	24.12 ± 1.48	33.14 ± 1.8	-19.717	**<0.001****
WC (cm)	77.12 ± 8.31	105.77 ± 18.27	-3.942	**<0.001****
WHR	0.8 ± 0.17	0.88 ± 0.11	-7.278	**<0.001****
Systolic blood pressure (mmHg)	116.54 ± 19.9	134.46 ± 23.01	-3.655	**<0.001****
Diastolic blood pressure (mmHg)	65.77 ± 7.58	74.81 ± 10.15	-3.64	**<0.001****
Laboratory data				
Serum urea (mg/dl)	41.15 ± 9.43	39.58 ± 6.64	0.697	0.489
Serum creatinine (mg/dl)	0.78 ± 0.14	0.79 ± 0.14	-0.197	0.845
HbA1c (%)	5.08 ± 0.45	5.35 ± 0.51	-2.047	**0.046***
Fasting blood glucose (mg/dl)	93.88 ± 3.24	94.92 ± 3.85	-1.053	0.298
2 hours postprandial blood glucose (mg/dl)	123.69 ± 8.06	130.77 ± 11.94	-2.505	**0.016***
Fating insulin (µU/mL)	8.72 ± 1.79	14.2 ± 4.12	-8.076	**<0.001****
HOMA-IR	2.03 ± 0.47	3.27 ± 0.18	-5.395	**<0.001****
Meteorin-like protein (ng/ml)	2.98 ± 0.81	4.49 ± 1.35	-4.879	**<0.001****

HbA1c: glycated hemoglobin, HOMA-IR: homeostatic model assessment -insulin resistance, BMI: body mass index, WC:waist circumflex, WHR:waist to hip ratio.

χ^2Chi square test, t independent sample t test, *: Significant, **: Highly significant ¥data is represented as median and interquartile range and compared using Mann Whitney test

Table 3 shows that there was a statistically significant rise in weight, body mass index, waist circumference, waist to hip ratio, and systolic blood pressure when obese diabetic patients were compared to non-obesity diabetic patients. Obese and non-obese diabetic patients did not differ statistically significantly in terms of gender, age, height, or diastolic blood pressure. Obese diabetes patients had significantly greater fasting insulin, HOMA-IR, and serum meteorin-like protein levels compared to non-obese diabetic patients, while having significantly lower blood urea levels. There was no statistically significant difference between obese and non-obese diabetes patients in serum creatinine, HbA1c, fasting blood sugar, or 2-hour postprandial blood sugar**.**

Table (3): Comparison between non-obese and obese diabetic patient groups regarding demographic and clinical data

	Non-obese diabetic group N=26(%)	Obese diabetic group N=26(%)	χ^2	P
Gender: Female / **Male**	15 (57.7%) / 11 (42.3%)	16 (61.5%) / 10 (38.5%)	0.08	0.777
	Mean ± SD	**Mean ± SD**	**T**	**P**
Age (year)	51.65 ± 12.52	51.38 ± 12.37	0.078	0.938
Height (cm)	166.42 ± 6.16	164.15 ± 7.0	1.241	0.22
Weight (kg)	68.92 ± 8.37	91.27 ± 8.27	-9.684	**<0.001****
BMI (kg/m^2)	24.52 ± 1.27	33.81 ± 2.4	-17.468	**<0.001****
WC (cm)	85.23 ± 6.42	103.12 ± 13.52	-6.094	**<0.001****
WHR	0.82 ± 0.15	0.93 ± 0.13	-2.885	**0.007***
Systolic blood pressure (mmHg)	133.08 ± 10.01	150.62 ± 15.63	-4.818	**<0.001****
Diastolic blood pressure (mmHg)	79.23 ± 8.91	82.69 ± 12.1	-1.174	0.246
Laboratory data				
Serum urea (mg/dl)	45.12 ± 7.52	40.65 ± 7.81	2.097	**0.041***
Serum creatinine (mg/dl)	0.79 ± 0.14	0.78 ± 0.14	0.814	0.419
HbA1c (%)	8.37 ± 1.17	8.35 ± 1.37	0.054	0.957
Fasting blood glucose (mg/dl)	159.31 ± 34.62	153.08 ± 20.29	0.792	0.432
2 hours postprandial blood glucose (mg/dl)	228.69 ± 18.3	219.08 ± 19.49	1.834	0.073
Fating insulin (µU/mL)	14.4 ± 3.2	20.91 ± 5.44	**-5.266**	**<0.001****
HOMA-IR	5.92 ± 1.57	8.48 ± 2.59	-4.314	**<0.001****
Meteorin-like protein (ng/ml)	5.96 ± 1.93	7.45 ± 1.61	**-2.354**	**0.023***

HbA1c: glycated hemoglobin, HOMA-IR: homeostatic model assessment -insulin resistance, BMI: body mass index, WC:waist circumflex, WHR:waist to hip ratio. χ^2Chi square test, t independent sample t test, *: Significant, **: Highly significant ¥data is represented as median and interquartile range and compared using Mann Whitney test

Table 4; shows that there was statistically significant positive correlation between serum meteorin and all of age, BMI, weight, WC, SBP, DBP, HbA1c, fasting insulin, 2-hour postprandial blood glucose, and HOMA-IR. There was no statistically significant relationship between serum urea, creatinine, and WHR and serum meteorin.-like protein

Table (4): Correlation between serum meteorin and the studied parameters

	r	P
Age (year)	0.276	0.005*
Height (cm)	-0.203	0.039*
Weight (kg)	0.272	0.005*
BMI (kg/m^2)	0.404	<0.001**
WC (cm)	0.375	<0.001**
WHR	0.16	0.092
Systolic blood pressure (mmHg)	0.374	<0.001**
Diastolic blood pressure (mmHg)	0.233	0.017*
Serum urea (mg/dl)	0.042	0.672
Serum creatinine (mg/dl)	0.055	0.579
HbA1c (%)	0.574	<0.001**
Fasting blood glucose (mg/dl)	0.681	<0.001**
2 hours postprandial glucose(mg/dl)	0.659	<0.001**
Fating insulin (mU/L)	0.493	<0.001**
HOMA-IR	0.669	<0.001**

HbA1c: glycated hemoglobin, HOMA-IR: homeostatic model assessment -insulin resistance, BMI: body mass index, WC:waist circumflex, WHR:waist to hip ratio. r: Spearman rank correlation coefficient, *: Significant, **: Highly significant

BMI and fasting blood glucose are two parameters that were significantly and independently connected with serum meteorin-like protein as indicated in table 5.

Table (5): Linear stepwise regression analysis of factors significantly correlated to serum meteorin-ike protein in studied patients

	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval	
	β	Std. Error	Beta			Lower	Upper
(Constant)	-5.158	1.037		-4.971	<0.001**	-7.216	-3.100
Fasting blood glucose (mg/dl)	0.043	0.004	0.652	10.114	<0.001**	0.035	0.052
BMI (kg/m^2)	0.172	0.032	0.348	5.404	<0.001**	0.109	0.236

**: Highly significant

DISCUSSION

In the current investigation, we discovered that individuals with newly diagnosed T2DM had considerably greater serum meteorin-like protein levels than nondiabetic controls.

Regarding obesity, our findings showed that obese non-diabetic controls' serum meteorin levels were considerably greater than those of non-obese non-diabetic controls. Additionally, compared to nonobese diabetic individuals, obese diabetic patients had considerably greater serum meteorin-like protein levels.

Interestingly, the highest serum meteorin levels were found in obese T2DM patients as the elevated serum meteorin-like protein levels in T2DM individual were further exacerbated by obesity.

Our findings are consistent with numerous studies that were conducted to assess the involvement of proteins like meteorins in T2DM and obesity. **Chung *et al.*** [9] **and Wang *et al.*** [10] reported that patients' serum levels of meteorin considerably rose with newly diagnosed T2DM and may exacerbate insulin resistance and its dependence in T2DM in human patients.

Similarly**, AlKhairi *et al.*** [11] discovered that serum meteorin levels were elevated in both obese and T2DM patients, and that these levels are further aggravated in obese T2DM patients, which was consistent with our investigation**.**

The increased level of meteorin in patients with type 2 diabetes and people without diabetes who are obese, could be a physiological attempt to reestablish glucose tolerance or a protective mechanism against metabolic stress or resistance to meteorin-like protein, like hyperinsulinemia and hyperleptinemia that occur with insulin and leptin resistance [9].

Inhibiting the production of peroxisome proliferator-activated receptor gamma (PPARγ) overexpression of the meteorin-like protein was found to cause hyperinsulinemia and insulin resistance in human adipocytes [12]**.** Consequently, medicine that blocks PPAR gamma signaling may have an impact on the amount in the blood of meteorin- like protein. In our study T2DM patients were newly diagnosed and did not receive any medication.

In line with our findings, elevated serum levels of the meteorin-like protein may raise the risk of T2DM through fostering insulin resistance. A preventive compensatory response to metabolic excess, including insulin resistance, may be another reason why people with T2DM have higher serum levels of the protein meteorin-like [9]**.** Meteorin -like protein is serum levels of the meteorin-like protein, which is abundantly white adipose tissue expresses, were linked with body mass index (BMI) and waist circumference (WC) as indicators of obesity in our investigation. According to the study's findings, obese people had higher serum levels of a protein resembling meteorin than non-obese participants did.

Löffler *et al.* [12] reported that obese children expressed more meteorin-like protein in their adipocytes than thin youngsters and this is in agreement with the present study**.**

On other hand, **Chung *et al.*** [9] discovered that serum meteorin-like protein levels did not correlate with body weight, BMI, waist circumference, or fat tissue mass. In clinical research, confounding variables like age, sex, medications, and physical activity may also contribute to this disparity**.**

The findings of the current study are in agreement with **Wang *et al.***'s study, which discovered a positive correlation between serum meteorin-like protein, fasting insulin, and HOMA-IR, a measure of insulin resistance, which was the first to show a significant positive correlation between serum meteorin-like protein and insulin resistance and suggested that meteorin-like protein might contribute to the development of T2DM dependent on insulin resistance in human subpopulations [10].

our result showed that there is a positive correlation between serum meteorin-like protein and Fasting blood glucose, HbA1C and this was in agreement with AlKhairi et al study**.**

Using stepwise multivariate logistic based on a regression analysis, BMI and fasting blood sugar were significantly independently associated with serum meteorin-like protein level in studied patients.

CONCLUSION

This study showed that newly diagnosed cases of T2DM and obesity have higher levels of circulating blood meteorin-like proteins. Furthermore, there was a significant positive connection between serum levels of meteorin-like proteins and BMI, WC, FBG, HbA1C, fasting insulin, and HOMA-IR. Future research is required, therefore, to shed light on the variables affecting the blood levels of meteorin-like protein, a brand-new medicinal compound and prognostic biomarker to treat obesity and T2DM risk factors.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest: There are no conflicts of interest, according to the authors.

REFERENCES

1. **Sapra A, Bhandari P (2022):** Diabetes Mellitus. In: StatPearls. Treasure Island (FL)., StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK553213/
2. **da Rocha J, Ogurtsova K, Linnenkamp U *et al.* (2016):** IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. *Diabetes research and clinical practice*, *117*: 48-54.
3. **American Diabetes Association (2022):** Introduction: Standards of medical care in diabetes-2022. Diabetes Care, 45 (1): S1-S2.
4. **Mastebhakti B, Gupta N, Singh S *et al.* (2020):** Epicardial adipose tissue thickness as a reliable marker of increased cardiovascular risk in patients with type 2 diabetes mellitus. Journal of Endocrinology & Metabolism, 10 (6):173-181.
5. **Zamora-Mendoza R, Rosas-Vargas H, Ramos-Cervantes T *et al.* (2018):** Dysregulation of mitochondrial function and biogenesis modulators in adipose tissue of obese children. Int J Obes., 42(4):618–24.
6. **Cheng H, Tsao C, Tzeng S *et al.* (2017):** Body mass index and waist circumference are better predictors of insulin resistance than total body fat percentage in middle-aged and elderly Taiwanese. Med (United States), 96(39):1–6.
7. **Ahima S, Lazar A (2013):** Physiology. The health risk of obesity – better metrics imperative. Science, 341:856–858.
8. **Rao R, Long Z, White P *et al.* (2014):** Meteorin-like is a hormone that regulates immune-adipose interactions to increase beige fat thermogenesis. Cell, 157: 1279–1291.
9. **Chung S, Hwang Y, Choi H *et al.* (2018):** Implications of circulating Meteorin-like (Metrnl) level in human subjects with type 2 diabetes. Diabetes Res Clin Pract., 136: 100–107.
10. **Wang K, Li F, Wang C *et al.* (2019):** Serum levels of meteorin-like (Metrnl) are increased in patients with newly diagnosed type 2 diabetes mellitus and are associated with insulin resistance. *Medical science monitor: international medical journal of experimental and clinical research*, *25:* 23-37.
11. **AlKhairi I, Cherian P, Abu-Farha *et al.* (2019):** Increased expression of meteorin-like hormone in type 2 diabetes and obesity and its association with irisin. *Cells*, *8*(10): 1283.
12. **Löffler D, Landgraf K, Rockstroh D *et al.* (2017):** METRNL decreases during adipogenesis and inhibits adipocyte differentiation leading to adipocyte hypertrophy in humans. International journal of obesity, 41(1): 112-119.