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Research Article

Low serum levels of meteorin-like/subfatin is related to obesity and insulin resistance

Düşük serum meteorin benzeri/subfatin seviyesi, obezite ve insülin direnci ile ilişkilidir

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Abstract

Introduction: Meteorin-like (Metrnl), also known as subfatin is a newly discovered adipokine of adipocyte origin that may play a role in obesity and insulin resistance. The current study aimed to investigate the association between subfatin and biochemical values, demographic characteristics, and insulin resistance in obese patients and healthy controls.

Methods: This cross-sectional study included 59 obese patients with sex and age-matched group of 41 healthy controls. An enzyme-linked immunosorbent assay (ELISA) was used to measure the serum levels of Subfatin (Metrnl), and the correlations of Metrnl level with anthropometric parameters, HOMA index, and biochemical measurements were assessed.

Results: The levels of BMI (p<0.001), insulin (p=0.002), and HOMA-IR score (p<0.001) were significantly higher in obese patients than controls. The serum levels of Subfatin were found to be lower in obese patients (1.85 [1.35–5.51] ng/ml) compared to the healthy controls (21.82 [12.61–27.76] ng/ml) (p<0.001). Subfatin had a significantly negative relationship with age (r =-0.250, p=0.012), weight (r =-0.373, p=0.001), BMI (r =-0.492, p=0.001), HbA1c (r =-0.209, p=0.037), LDL (r =-0.264, p=0.008), HOMA-IR (r =-0.223, p=0.026), and glucose (r =-0.376, p<0.001). There was a significantly positive correlation between subfatin and height (r=0.321, p=0.001).

Conclusion: These results show that levels of subfatin were decreased in obese patients. There is a relationship between circulating amounts of subfatin hormone and age, weight, height, LDL-cholesterol, glucose, hbA1c, and HOMA-IR. Subfatin might be a new biomarker of obesity and insulin resistance.

Keywords: Meteorin-like/subfatin, adiposity, insulin resistance, adipokines, biomarkers, diabetes mellitus type 2

Öz

Giriş: Subfatin olarak da bilinen Meteorin benzeri (Metrnl), obezite ve insülin direncinde rol oynayan ve yeni keşfedilen adiposit kökenli bir adipokindir. Bu çalışma obez hastalarda ve sağlıklı kontrollerde subfatin ile biyokimyasal değerler, demografik veriler ve insülin direnci değerleri arasındaki ilişkiyi araştırmayı amaçlamıştır.

Yöntem: Bu kesitsel çalışmaya cinsiyet ve yaş açısından eşleştirilmiş 41 sağlıklı kontrol ile 59 obez hasta dahil edildi. Subfatin'in (Metrnl) serum seviyelerini ölçmek için bir enzime bağlı immünosorbent tahlili (ELISA) kullanıldı ve Metrnl seviyesinin antropometrik parametreler, HOMA indeksi ve biyokimyasal ölçümlerle korelasyonları değerlendirildi.

Bulgular: Obez hastalarda BKİ (p<0,001), insülin (p=0,002) ve HOMA-IR skoru (p<0,001) düzeyleri kontrollere göre anlamlı derecede yüksekti. Subfatin serum seviyeleri obez hastalarda (1,85 [1,35-5,51] ng/ml) sağlıklı kontrollere (21,82 [12,61-27,76] ng/ml) göre daha düşük bulundu (p<0,001). Subfatin ile yaş (r=-0,250, p=0,012), ağırlık (r=-0,373, p<0,001), BKİ (r=-0,492, p<0,001), HbA1c (r=-0,209, p=0,037), LDL (r=-0,264, p=0,008), HOMA-IR (r=-0,223, p=0,026), glukoz (r=-0,376, p<0,001) arasında negatif anlamlı korelasyon saptandı. Boy (r=0,321, p=0,001) ile subfatin arasında anlamlı pozitif korelasyon saptandı.

Sonuç: Bu sonuçlar, obez hastalarda subfatin düzeylerinin azaldığını göstermektedir. Dolaşımdaki subfatin hormonu miktarları ile yaş, kilo, boy, LDL-kolesterol, glukoz, hbA1c ve HOMA-IR arasında bir ilişki vardır. Subfatin, obezite ve insülin direncinin yeni bir biyobelirteci olabilir.

Anahtar kelimeler: Meteorin benzeri/subfatin, yağlanma, insülin direnci, adipokinler, biyobelirteçler, tip 2 diyabetes mellitus

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Key Points

1. Circulating subfatin levels are decreased in obese individuals.
2. Serum Subfatin level was negatively correlated with BMI, weight, HbA1c, HOMA-IR, glucose, and LDL levels.
3. Serum subfatin level may be a new marker for insulin resistance and obesity.

Introduction

Due to its rapidly increasing prevalence like a snowball, obesity is now considered an epidemic disease. Adipose tissue, which increases with obesity, plays an important role in insulin resistance. The mechanisms involved in the development of insulin resistance in adipose tissue have not yet been fully elucidated. Adipose tissue, known as a tissue, where excess energy is stored in the form of triglycerides, has now been shown to be an endocrine organ that produces and secretes adipokines. It is known that adipose tissue plays an important role in the regulation of many mechanisms, such as metabolic hemostasis, insulin sensitivity, inflammation and immunity through adipokines secreted by adipose tissue [1]. Chronic inflammation caused by obesity and increased adipokine secretion contributes to a very important role in the development of insulin resistance. In insulin-resistant states, there is continuous insulin production from the pancreas to balance glucose metabolism. Prolonged insulin resistance causes damage in pancreatic beta cells and an increase in blood glucose in the circulation, eventually leading to the development of diabetes. About 10 years before the diagnosis of type 2 diabetes mellitus (T2DM) in humans, insulin sensitivity decreases, insulin secretion increases, and blood glucose begins to increase as a result. Preventing insulin resistance caused by obesity is also essential for preventing type 2 diabetes mellitus [2, 3].

Subfatin (Meteorin-like protein; METRNL) is one of the newly discovered adipokines secreted from adipose and skeletal muscle tissue. It has been reported that subfatin increases insulin sensitivity and also has an anti-inflammatory effect [4, 5]. Studies in mice have shown that subfatin increases energy expenditure and insulin sensitivity [4]. Previous literature examining the relationship between subfatin and obesity differs. In the literature, it was reported that the subfatin level was lower in obese individuals [6], in another study, subfatin expression increased in obese children compared to lean children, and in another study, there was no difference in subfatin levels between obese and non-obese individuals [5, 7]. In three different studies in the literature, it has been shown that subfatin levels are lower in type 2 diabetic individuals compared to the control group [8-10]. These studies reported that low subfatin level may be associated with worsening glucose tolerance and there is a negative correlation between Subfatin level and both insulin level and HOMA index.

The mechanisms described above and literature data show that there may be a relationship between subfatin and endocrine diseases. Changes in subfatin expression, especially as a result of increased body adiposity due to obesity, may have effects on insulin sensitivity and insulin resistance. The current study aimed to investigate both the difference in subfatin levels between obese and non-obese individuals and the possible relationship between subfatin levels and insulin resistance.

Methods

This cross sectional study was conducted on 59 obese and 41 non-obese healthy controls. Participants were selected from individuals aged 18-60 years who applied to the internal medicine outpatient clinic between November 2018 and September 2020. Patients with previously diagnosed T2DM, other types of diabetes, endocrine disease, severe cardiovascular or cerebrovascular diseases, severe liver or renal disease, and medication history including the use of antidiabetics, statins, diuretics, corticosteroids, estrogen, and progestin, which influence glucose tolerance and insulin sensitivity, obesity treatment and bariatric surgery were excluded. Obesity was diagnosed by a body mass index (BMI) ≥30.0 kg/m2 and non-obesity was diagnosed by a body mass index (BMI) <25.0 kg/m2 based on the criteria recommended by the WHO [11].

Anthropometric and biochemical measurements

Demographic data (age, sex, weight, height, waist and hip circumference measurements) were recorded. A standard formula (weight (kg) / height (m^2)) was used for the calculation of body mass index (BMI). Systolic blood pressure(SBP) and diastolic blood pressure (DBP) were determined after 15 minutes of rest. The measurement of systolic and diastolic blood pressure was performed three times by using a random zero sphygmomanometer. The mean numbers of blood pressure measurements was recorded. After overnight fasting, venous blood was collected from all participants. Fasting blood glucose (FBG), triglycerides (TG), total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and creatinine (Cr) were measured using commercially available kits (Pars Azmoon, Iran). Also, the ELISA technique was used for measuring fasting insulin levels (Monobind, USA). The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the following equation: [FBG (mg/dL)] × [fasting blood insulin (µU/mL)] / 405.

Serum level of subfatin (Meteorin-like Protein) was measured by the ELISA method in accordance with the study procedures specified in the catalogues (Human Meteorin-like Protein ELISA Kit Sunred Biotechnology Company, Cat No: 201-12-9252). The Intra-Assay: CV value of the subfatin kit was <8%, and the Inter-Assay: CV value was <10%. The measuring range (standard curve range) of the subfatin kit was 0.05–15 ng/mL, and the minimum measurable level (sensitivity) was 0.023 ng/mL. Analysis procedure; ***i)*** Standard dilutions; It was prepared by adding the standard solution and standard diluting solution in the kit amounts specified in the package leaflet. ***ii)*** Blank Well: The first well of the plate with 96 wells was left empty. Standard Wells: 50 µl of standard dilutions and 50 µl of streptavidin-horseradish peroxidase (horseradish peroxidase; HRP) were added. Test Wells: 40 µl of serum samples, 10 µl of specific antibody and 50 µl of streptavidin-HRP were added. ***iii)*** After the plate was covered with a sealer, it was gently shaken and incubated at 37 °C for 60 minutes. At the end of the time, the cover on the plate was removed and washed with the washing solution by diluting 30 times with distilled water for 1-2 minutes. The solution was poured, and the plate was dried on blotting paper. This step was repeated 5 times. ***iv)*** 50 µl of chromogen A and 50 µl of chromogen B solutions were added to each well and incubated at 37 °C for 60 minutes after shaking gently. ***v)*** Afterwards, 50 µl of Stop solution was added to each well and the transformation of blue color to yellow was observed. Optical density (OD) was measured at 450 nanometers (nm) in a microplate reader (Thermo Fisher Scientific, MultiscanTM FC Microplate Photometer, Cat No: 51119000).

Ethical approval, informed consent and permissions

The study protocol was approved by the Ethics Committee of Firat University (date: 25.10.2018, Approval number:17/06). A written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analysis of the data was performed by IBM SPSS 22 (SPSS Inc., Chicago, IL, USA) statistics package program. The distribution of continuous data was analyzed using the Shapiro-Wilk test. Descriptive data were given as mean ± SD for continuous variables with normal distribution, median (quartile 1-quartile 3) for continuous data with non-normal distribution, and number (n) and percentage (%) for categorical variables. For comparison of two independent groups, we used the Student t test for normally distributed continuous data and Mann Whitney-U test for non-normal distributed continuous data. Pearson Chi-square test was used to analyze categorical data. Pearson correlation analysis or Spearman correlation analysis were used to examine the relationship between continuous variables. A value of $p<0.05$ was considered statistically significant.

Results

Fifty-nine obese and forty-one non-obese healthy controls participated in the study. There were no significant differences in terms of age ($p = 0.152$), and sex ($p = 0.095$) between the studied groups. The levels of BMI ($p<0.001$), insulin ($p=0.002$), and HOMA-IR score ($p<0.001$) were significantly higher in obese patients than controls (Table 1).

Table 1. Demographic, anthropometric, and biochemical characteristics of participants

Variables	Obese n=59	Controls n=41	p value
Sex			
Female n (%)	49 (83.1)	30 (73.2)	0.233*
Male n (%)	10 (16.9)	11 (26.8)	
Age (year) Median (IQR)	39 (31-45)	33 (31-41)	0.164**
Height (cm) Median (IQR)	161.0 (158.0-165.0)	168.0 (161.0-174.0)	**<0.001****
Weight (kg) Median (IQR)	91.6 (83.0-100.0)	71.0 (62.0-79.0)	**<0.001****
BMI (kg/m^2) Median (IQR)	34.2 (31.3-38.6)	24.9 (23-26.8)	**<0.001****
Insulin (µIU/ml) mean±SD	12.8±5.8	9.6±4.6	**0.002****
HOMA-IR mean±SD	3.3±1.7	2.2±1.2	**<0.001****
HbA1c (%) mean±SD	5.5±0.5	5.5±0.4	0.978***
T. cholesterol (mg/dL) mean±SD	187.5±40.3	170.5±29.2	**0.023*****
LDL (mg/dL) mean±SD	120.8±36.5	99.0±24.6	**0.001*****
Glucose (mg/dL) Median (IQR)	97.0 (89.0-104.0)	91.0 (84.0-97.0)	**0.006****
Urea (mg/dL) Median (IQR)	23.0 (21.0-28.0)	25.0 (21.0-29.0)	0.284**
Creatinine (mg/dL) Median (IQR)	0.63 (0.56-0.72)	0.66 (0.58-0.81)	0.058**
AST (U/L) Median (IQR)	20.0 (17.0-25.0)	20.0 (16.0-24.0)	0.384**
ALT (U/L) Median (IQR)	19.0 (14.0-26.0)	17.0 (12.0-25.0)	0.171**

*Chi-square test. **Mann Whitney U test. ***Student t test. IQR: Interquartile Range. SD: Standard deviation. BMI: body mass index; LDL: low density lipoprotein.

The serum levels of Subfatin were found to be lower in obese group (1.85 [1.35-5.51] ng/ml) compared to healthy controls (21.82 [12.61-27.76] ng/ml) ($p<0.001$, Figure 1).

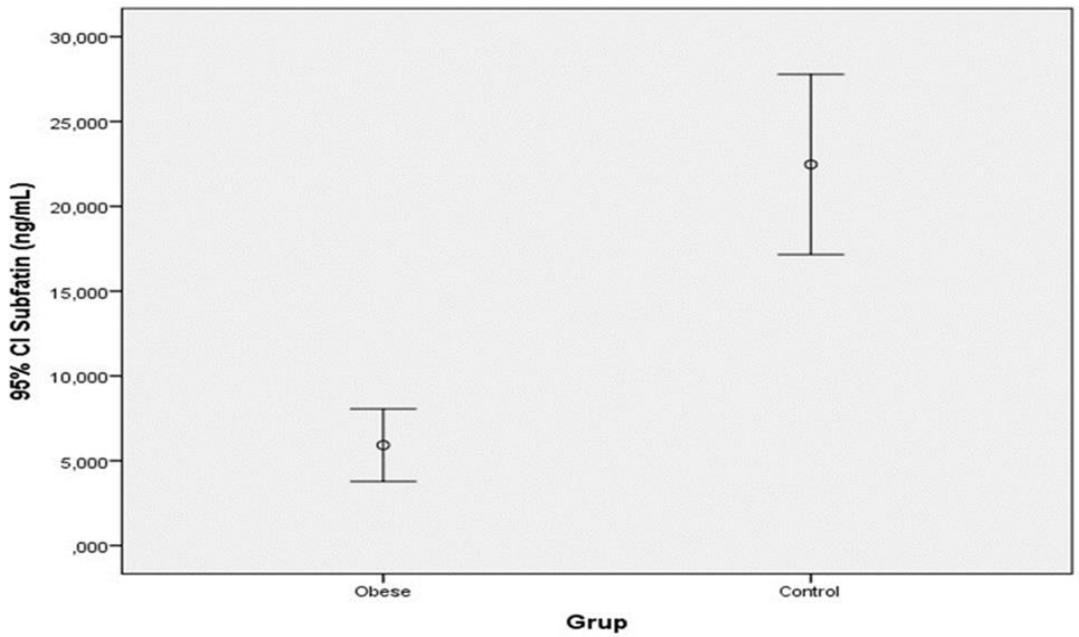

Figure 1. Comparison of subfatin levels between the obese patients and controls.

Subfatin was significantly negative associated with age (r=-0.250. p=0.012), weight (r=-0.373. p<0.001), BMI (r=-0.492. p<0.001), HbA1c (r=-0.209. p=0.037), LDL (r=-0.264. p=0.008), HOMA-IR (r=-0.223. p=0.026), glucose (r=-0.376. p<0.001). There was a significantly positive correlation between subfatin and height (r=0.321. p=0.001). (Table 2)

Table 2. Correlation of Subfatin with anthropometric and biochemical data.

	Subfatin (ng/mL)	
	r	p
Age	-0.250	**0.012**
Height (cm)	0.321	**0.001**
Weight (kg)	-0.373	**<0.001**
BMI (kg/m2)	-0.492	**<0.001**
Insulin (µIU/ml)	0.009	0.944
HOMA-IR	-0.077	0.560
HbA1c (%)	-0.209	**0.037**
T. cholesterol (mg/dL)	-0196	0.050
LDL (mg/dL)	-0.264	**0.008**
Insulin	-0.127	0.206
HOMA-IR	-0.223	**0.026**
Glucose (mg/dL)	-0.376	**<0.001**
Urea (mg/dL)	0.150	0.137
Creatinine (mg/dL)	0.148	0.142
AST (U/L)	-0.001	0.995
ALT (U/L)	-0.060	0.551

BMI: body mass index; LDL: low density lipoprotein.

Discussion

Adipose tissue is seen as an endocrine organ because it secretes various proteins and peptides called adipokines. Through adipokines secreted by adipose tissue, it performs numerous endocrine functions such as metabolic hemostasis, glucose metabolism, and insulin sensitivity [12]. The current study looked at the relationship between subfatin levels and obesity and metabolic parameters.

In the current study, the serum subfatin level was found to be lower in obese individuals. The relationship between obesity and subfatin levels is contradictory in the literature. Ugur et al. reported that there was no difference in subfatin levels between the obese and control groups [7]. Li et al. reported that the subfatin level increased in obese mice [13]. Alkhari et al. reported that the subfatin level was higher in obese compared to non-obese mice [14]. In these studies, confounding factors such as metabolic syndrome and type 2 diabetes mellitus in obese individuals drew the attention. Dadmanesh et al. reported that the subfatin level was lower in obese patients [10]. Consistent with our results, another study reported that subfatin levels were lower in obese patients scheduled for bariatric surgery compared to the control group and there was an increase in subfatin levels after bariatric surgery.

In the current study, a negative correlation was found between BMI and subfatin level. Similar to our findings, previous studies have shown that there is a negative correlation between subfatin and BMI [7, 9, 10, 15]. The negative correlation between subfatin and BMI can explain the low level of subfatin in obesity. Schmid et al. reported that weight loss is associated with an increased serum subfatin level in morbidly obese patients [16]. In line with previous research, the current study found that subfatin levels were low in obese people and negatively correlated with BMI. Previous studies showed that subfatin from subcutaneous white adipose tissue with relatively lower expression levels was found in brown adipose tissue and a much lower expression level in the brain [7]. Subfatin from adipose tissue is expected to be higher in obese patients, but it was found to be lower in the current study. A defect in subfatin secretion can lead to low serum subfatin levels and obesity. The lack of an increase in subfatin levels with the increase in adipose tissue may be associated with the release defect. In order to elucidate the relationship between obesity and subfatin, there is a need for new studies that will take into account the data we have obtained.

The current study showed that there was a significantly negative correlation between subfatin and HOMA-IR and glucose levels. There is varying evidence to suggest the positive effects of subfatin on insulin sensitivity. Zheng et al. reported that mice specifically overexpressing Metrnl in adipocytes were protected from diet-induced insulin resistance [17]. Many literature studies have reported that subfatin is associated with insulin resistance [9, 10, 16-18]. The current study showed that the serum subfatin level is lower in the obese group, and a low serum subfatin level increases insulin resistance. Wang. et al. reported that serum subfatin levels are increased in diabetic and prediabetic patients compared to controls [19]. The findings of Wang. et al. are contradictory to our findings. A previous rat study has shown that Subfatin in adipocytes could increase insulin sensitivity by stimulating the peroxisome proliferator-activated receptor gamma (PPARγ) pathway [13]. According to this mechanism, increased subfatin can reduce insulin resistance by increasing insulin sensitivity, which is consistent with our findings. On the basis of current results, the effect of Metrnl on insulin resistance should be confirmed by further studies as at this time. Studies on serum Metrnl and its association with obesity and insulin resistance are limited and the findings have been contradictory.

Limitations

This current study has some limitations. First, this is a cross-sectional study and may have failed to examine the role of subfatin in the developmental stage of obesity and insulin resistance. Subfatin is found in a variety of tissues, including adipose tissue, muscle tissue, the brain, and macrophages. The current study may have ignored these factors that will affect subfatin secretion. We suggest investigating the relationship between obesity development and subfatin level with prospective cohort studies.

Conclusion

The current study showed that a decreased subfatin level is associated with obesity. Furthermore, decreased serum subfatin level is associated with insulin resistance. The decreased subfatin secretion may be the cause of obesity, which is one of the most important health problems. New studies are needed to elucidate the role of subfatin in obesity and insulin resistance.

Conflict of interest: None

Author Contributions		Author Initials
SCD	Study Conception and Design	CC, EO, ED, EO
AD	Acquisition of Data	CC, IB
AID	Analysis and Interpretation of Data	BY, EO
DM	Drafting of Manuscript	BY, EO, CC, ED, EO, IB
CR	Critical Revision	BY, EO, CC, ED, EO, IB

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References

1. Ahmed B, Sultana R, Greene MW. Adipose tissue and insulin resistance in obese. Biomed Pharmacother. 2021;137:111315. https://doi.org/10.1016/j.biopha.2021.111315
2. Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk state for diabetes development. Lancet. 2012;379(9833):2279-90. https://doi.org/10.1016/s0140-6736(12)60283-9
3. Kahn SE, Hull RL. Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121):840-6. https://doi.org/10.1038/nature05482
4. Rao RR, Long JZ, White JP, Svensson KJ, Lou J, Lokurkar I, et al. Meteorin-like is a hormone that regulates immune-adipose interactions to increase beige fat thermogenesis. Cell. 2014;157(6):1279-91. https://doi.org/10.1016/j.cell.2014.03.065
5. Löffler D, Landgraf K, Rockstroh D, Schwartze JT, Dunzendorfer H, Kiess W, et al. METRNL decreases during adipogenesis and inhibits adipocyte differentiation leading to adipocyte hypertrophy in humans. Int J Obes (Lond). 2017;41(1):112-9. https://doi.org/10.1038/ijo.2016.180
6. Pellitero S, Piquer-Garcia I, Ferrer-Curriu G, Puig R, Martínez E, Moreno P, et al. Opposite changes in meteorin-like and oncostatin m levels are associated with metabolic improvements after bariatric surgery. Int J Obes (Lond). 2018;42(4):919-22. https://doi.org/10.1038/ijo.2017.268
7. Ugur K, Erman F, Turkoglu S, Aydin Y, Aksoy A, Lale A, et al. Asprosin. visfatin and subfatin as new biomarkers of obesity and metabolic syndrome. Eur Rev Med Pharmacol Sci. 2022;26(6):2124-33. https://doi.org/10.26355/eurrev_202203_28360
8. El-Ashmawy HM, Selim FO, Hosny TAM, Almassry HN. Association of low serum Meteorin like (Metrnl) concentrations with worsening of glucose tolerance. impaired endothelial function and atherosclerosis. Diabetes Res Clin Pract. 2019;150:57-63. https://doi.org/10.1016/j.diabres.2019.02.026
9. Onalan E, Cavlı C, Dogan Y, Onalan E, Gozel N, Buran I, et al. Low serum levels of meteorin-like/subfatin: an indicator of diabetes mellitus and insulin resistance? Endokrynol Pol. 2020;71(5):397-3. https://doi.org/10.5603/ep.a2020.0038
10. Dadmanesh M, Aghajani H, Fadaei R, Ghorban K. Lower serum levels of Meteorin-like/Subfatin in patients with coronary artery disease and type 2 diabetes mellitus are negatively associated with insulin resistance and inflammatory cytokines. PLoS One. 2018;13(9):e0204180. https://doi.org/10.1371/journal.pone.0204180
11. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii. 1-253. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
12. Booth A, Magnuson A, Fouts J, Foster MT. Adipose tissue: an endocrine organ playing a role in metabolic regulation. Horm Mol Biol Clin Investig. 2016;26(1):25-42.
13. Li ZY, Song J, Zheng SL, Fan MB, Guan YF, Qu Y, et al. Adipocyte Metrnl Antagonizes Insulin Resistance Through PPARγ Signaling. Diabetes. 2015;64(12):4011-22. https://doi.org/10.2337/db15-0274
14. AlKhairi I, Cherian P, Abu-Farha M, Madhoun AA, Nizam R, Melhem M, et al. Increased Expression of Meteorin-Like Hormone in Type 2 Diabetes and Obesity and Its Association with Irisin. Cells. 2019;8(10):1283. https://doi.org/10.3390/cells8101283
15. Fadaei R, Dadmanesh M, Moradi N, Ahmadi R, Shokoohi NA, Aghajani H, et al. Serum levels of subfatin in patients with type 2 diabetes mellitus and its association with vascular adhesion molecules. Arch Physiol Biochem. 2020;126(4):335-40. https://doi.org/10.1080/13813455.2018.1538248
16. Schmid A, Karrasch T, Schäffler A. Meteorin-Like Protein (Metrnl) in Obesity. during Weight Loss and in Adipocyte Differentiation. J Clin Med. 2021;10(19):4338. https://doi.org/10.3390/jcm10194338
17. Zheng SL, Li ZY, Song J, Liu JM, Miao CY. Metrnl: a secreted protein with new emerging functions. Acta Pharmacol Sin. 2016;37(5):571-9. https://doi.org/10.1038/aps.2016.9
18. Alizadeh H, Alizadeh A. Association of Meteorin-Like Hormone with insulin resistance and body composition in healthy Iranian adults. Diabetes Metab Syndr. 2020;14(5):881-85. https://doi.org/10.1016/j.dsx.2020.05.031
19. Wang K, Li F, Wang C, Deng Y, Cao Z, Cui Y, et al. Serum Levels of Meteorin-Like (Metrnl) Are Increased in Patients with Newly Diagnosed Type 2 Diabetes Mellitus and Are Associated with Insulin Resistance. Med Sci Monit. 2019;25:2337-43. https://doi.org/10.12659/msm.915331