International Journal of Nutrology
(Official Journal of the ABRAN - Brazilian Association of Nutrology)

ORIGINAL ARTICLE

DOI: 10.54448/ijn26313

Spexin and Nesfatin-1 as predictive biomarkers of insulin resistance and type 2 diabetes risk in adults with obesity: a cross-sectional study

Zainab Pasha Ibrahim[1,*], Sahib Jumaah Abdul Rahman[1]

[1] University of Kirkuk. College of Education for Pure Sciences. Department of Life Sciences, Kirkuk, Iraq.

*Corresponding author: Zainab Pasha Ibrahim.
College of Education for Pure Sciences / Department of Life Sciences / University of Kirkuk / Kirkuk / Iraq.
E-mail: epbm24013@uokirkuk.edu.iq
DOI: https://doi.org/10.54448/ijn26313
Received: 01-10-2026; Revised: 02-20-2026; Accepted: 02-24-2026; Published: 07-23-2026; IJN-id: e26313

Editor: Dr. Idiberto José Zotarelli-Filho, MSc, Ph.D., Post-Doctoral.

Abstract

Introduction: Type 2 diabetes mellitus (T2DM) and obesity are among the most pressing global public health concerns. The prevalence of obesity has increased markedly worldwide over recent decades, while T2DM currently affects more than 530 million adults, with projections indicating a continued rise in its global burden in the coming years. **Objective**: The present study was conducted to determine Spexin and Nesfatin-1 serum levels in men with obesity compared with healthy individuals, their relation with insulin resistance estimated by HOMA-IR index and predictive value for insulin resistance and T2DM risk among obese subjects. **Materials and Methods**: 60 male subjects with obesity were recruited in the study, divided into three age groups (25–35, 36–45 and 46–55 years), together with thirty healthy male controls. Blood samples were obtained after fasting for at least 10 h. HOMA-IR was calculated for evaluation of insulin resistance, Spexin and Nesfatin-1 levels were determined by ELISA. Statistical tests were also carried out to compare groups, correlations and predictive value of the biomarkers studied. **Results**: There was a significant decrease ($p \leq 0.01$) in Spexin and Nesfatin-1 serum concentrations among Men with obesity compared to the control group. Both hormones presented significantly negative correlations with HOMA-IR, whilst fasting insulin and glucose were markedly higher ($p \leq 0.01$) in obese participants and that Spexin, Nesfatin-1 are inversely related to insulin resistance in OB. There were no differences in Spexin, Nesfatin-1 or insulin according to the age groups. In contrast, fasting plasma glucose and insulin resistance values showed impressively higher differences with aging ($p \leq 0.01$), exhibiting a very fecund progressive increase along the life span. **Conclusion**: The results indicate that Spexin and Nesfatin-1 might have potential predictive value for insulin resistance, and be Auxiliary biomarkers to early estimate the risk of T2DM in patients with obesity.

Keywords: Obesity. Nesfatin-1. Spexin. Insulin resistance. HOMA-IR. Type 2 diabetes mellitus.

Introduction

Obesity has emerged as one of the most critical public health challenges of the 21st century, with its prevalence increasing at an alarming rate worldwide. In 2022, more than one billion individuals were affected by obesity (BMI ≥ 30 kg/m²), accounting for approximately one in every eight adults globally, while nearly 43% of the adult population was classified as overweight or obese **[1]**. Parallel to this trend, the global burden of diabetes continues to rise substantially. According to the International Diabetes Federation, approximately 537 million adults were living with diabetes in 2021, and this number is projected to reach 783 million by 2045 **[2]**.

Obesity markedly increases the risk of developing a wide range of chronic disorders, including type 2 diabetes mellitus (T2DM), cardiovascular diseases, non-alcoholic fatty liver disease, musculoskeletal complications, certain psychological disturbances, and several types of cancer. Importantly, these adverse health outcomes cannot be attributed solely to excess fat accumulation; rather, they are largely driven by adipose tissue dysfunction, characterized by chronic low-grade inflammation and altered secretion of

adipokines and peptide hormones that disrupt metabolic homeostasis across multiple organ systems [3]. Body mass index (BMI) remains one of the most widely used anthropometric indicators for assessing obesity and estimating the risk of metabolic and cardiovascular diseases in clinical and epidemiological settings [4].

Insulin resistance represents a central pathophysiological mechanism linking obesity to the development of T2DM. It is defined by a diminished cellular responsiveness to insulin and is accompanied by profound disturbances in glucose and lipid metabolism. Moreover, insulin resistance is strongly associated with an increased long-term risk of cardiovascular morbidity and mortality, underscoring the importance of its early identification in obese individuals to mitigate the progression of diabetes and its complications [5].

In recent years, increasing attention has been directed toward peptide hormones involved in appetite regulation and energy homeostasis as potential biomarkers of metabolic dysfunction. Spexin, an evolutionarily conserved peptide, has been implicated in the regulation of energy balance through newly identified hypothalamic pathways, suggesting a significant role in metabolic control [6].

Experimental and clinical evidence further indicates that Spexin expression may be altered in obesity and modulated by therapeutic interventions such as aerobic exercise and metformin treatment [7]. Similarly, Nesfatin-1 was initially identified as a hypothalamic satiety-inducing peptide [8], and subsequent studies have expanded interest in this hormone due to its diverse metabolic, cardiovascular, and endocrine effects, as well as its potential involvement in metabolic disorders [9].

Despite the growing recognition of Nesfatin-1 and Spexin as important regulators of energy homeostasis, the current body of evidence remains fragmented and inconclusive. Most previous investigations have focused primarily on experimental models or descriptive physiological roles, while relatively few studies have evaluated their predictive value for insulin resistance in human obesity [6-10]. Furthermore, limited research has simultaneously examined both peptides in relation to insulin resistance indices such as the homeostasis model assessment of insulin resistance (HOMA-IR), and age-related variations among obese adults have been largely overlooked [7]. Consequently, the combined role of Nesfatin-1 and Spexin as early predictive biomarkers for insulin resistance and future T2DM risk in obese adult men remains insufficiently characterized.

Addressing this knowledge gap is essential to clarify whether these peptide hormones could serve as reliable early indicators of metabolic deterioration in obesity. Therefore, the present study aimed to assess serum levels of Spexin and Nesfatin-1 in Men with obesity compared with healthy controls across different age groups, and to investigate their associations with insulin resistance using the HOMA-IR index.

Materials and Methods

Study Design

This cross-sectional study evaluated the serum levels of Spexin and Nesfatin-1 in Men with obesity compared with healthy controls and investigated the relationship of these neuropeptides with insulin resistance. The study was designed and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure comprehensive and transparent reporting of observational data.

Study Samples

The sample for the current research comprised 90 men, aged 25–55 years. Sampling was conducted from early September to late November 2025 in Kirkuk City. Participants were classified into two groups: the obese group (BMI ≥ 30 kg/m²), further divided into three age categories (25–35, 36–45, and 46–55 years), and a control group consisting of 30 healthy men with normal BMI (18.5 < BMI < 24.9 kg/m²), age-matched to the obese participants. Those with a history of diabetes mellitus, chronic liver, or kidney diseases were excluded from the study. The sample size of 90 participants was selected to ensure adequate statistical power for detecting differences between obese and healthy participants. A one-way ANOVA test was planned for comparisons among groups, and this sample size was determined sufficient to achieve reliable and statistically significant results at a conventional significance level ($p \leq 0.01$).

Anthropometric Measurements

Weight and height were recorded according to conventional methods. Body mass index (BMI) was derived as body weight (kg)/ height (m^2) according to standard procedure [11].

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m}^2\text{)}}$$

Laboratory Analyses

Fasting blood glucose was measured in enzymatic Trinder technique [12] through serum using oxidation of glucose. The insulin resistance (IR) was estimated

by Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), which can be calculated using the following equation: fasting blood glucose level (mg/100 mL) × fasting serum insulin concentration(mU/L) ÷ 405 **[13]**.

$$\text{HOMA-IR} = \frac{\text{Fasting Blood Glucose} \times \text{Fasting Insulin}}{405}$$

Measurement of Nesfatin-1, Spexin, and Insulin Levels

Serum levels of Nesfatin-1, Spexin, and insulin were determined using the sandwich enzyme-linked immunosorbent assay (Sandwich ELISA) technique. The Micro ELISA plates supplied with the assay kits were pre-coated with specific antibodies against the target hormones. Standard solutions or serum samples were added to the appropriate wells and allowed to bind to the immobilized antibodies. Subsequently, HRP–streptavidin conjugate, specific for each hormone, was added to each well, followed by incubation.

After incubation, the wells were washed with wash buffer to remove unbound antibodies. Tetramethylbenzidine (TMB) substrate solution was then added to each well containing the antibody–HRP complex, resulting in the development of a blue color, which turned yellow after the addition of the stop solution. The optical density (OD) was measured spectrophotometrically at a wavelength of 450 nm, and the OD values were directly proportional to the concentrations of the respective hormones in the samples.

Statistical Analysis

The results were statistically analyzed using the Statistical Package for the Social Sciences (SPSS). The independent samples t-test was applied to compare the mean values between patients and healthy controls at a significance level of ($p \leq 0.01$). The values of the studied variables were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was used to compare the mean values across different age groups at a significance level of ($p \leq 0.01$). All variables were presented as mean ± standard deviation (SD).

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Scientific Research Ethics Committee of the Department of Biology, College of Education for Pure Sciences, University of Kirkuk (Approval Ref: BCPSKU/007/007H; Date: 5 August 2025). All research procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant international ethical guidelines. Written informed consent was obtained from all participants prior to their inclusion in the study, and confidentiality and privacy of participants' data were strictly maintained.

Results

Spexin

The serum Spexin levels were significantly decreased ($p \leq 0.01$) in the Men with obesity (638.27 ± 58.12 pg/mL) compared with those of the control group (860.33 ± 28.79 pg/mL). Regarding the age distribution, there were no statistically significant differences among the different age groups ($p \leq 0.01$). The mean spexin levels in (25–35) years group, (36-–45) years group and the (46–55) years group were (668.36 ± 55.54) pg/mL, (604.20 ±61.47) pg/mL and (642.25 ±57.35) p/mL respectively.

Nesfatin-1

Men with obesity had lower ($p \leq 0.01$) levels of Serum Nesfatin-1 (195.65 ± 25.66) pg/mL vs. (247.99 ± 36.93) pg/mL for the control . When age stratification was taken under consideration, no significant differences were found among all the ages ($p \leq 0.01$). The mean Nesfatin-1 levels were (201.39 ± 26.89) pg/mL in the age group of (25–35) years, (180.72 ± 21.19) pg/mL in the age group of (36-45) years, and (204.84 ± 28.92) pg/mL in the age group of (46–55 years).

Insulin

Men with obesity had higher ($p \leq 0.01$) serum insulin values (11.24 ± 1.36 mU/L) than the control group (6.80 ± 1.82 mU/L). In terms of age classification, no statistically significant differences were found between the age groups ($p \leq 0.01$). The average insulin levels were (12.38 ± 1.27) mU/L for the (25–35) year group, (10.80 ± 1.22) mU/L for the middle age group (36–45 years), and (10.56 ± 1.60) mU/L for the old age group (46–55 years).

Glucose

The fasting glucose was found to be significantly higher ($p \leq 0.01$) in obese males (186.73 ± 7.16 mg/100 mL) when compared to that of the control group (85.50 ± 2.99 mg/100 mL). There were significant differences among the age groups of patients for glucose ($p \leq 0.01$) and the glucose levels were increased progressively with increasing age: (169.03 ± 5.44) mg/100mL in the group of patients aged between (25–35) years, (186.31 ±6.08) mg/100mL in those between (36-45) years, and (204.86 ± 9.96) mg/100ml in those between (46-55) years.

HOMA-IR

Men with obesity presented a higher ($p \leq 0.01$) HOMA-IR index (5.33 ± 1.07) as compared to the control group (1.42 ± 0.87). Age-related differences were also significant ($p \leq 0.01$) HOMA-IR values increased steadily with age (3.01 ± 0.38) for subjects aged (25–35) years, (4.80 ± 0.45) for those aged from the fourth to fifth decade of life, and up to a maximum of (5.20 ± 0.24) in the last decade of life (46–55 years-old).

Body Mass Index (BMI)

Significantly higher ($p \leq 0.01$) body mass index (BMI) were found in the obese group participants (32.87 ± 2.44 kg/m²) than that of the control group participants (23.36 ± 1.74 kg/m²). In terms of age distribution, no statistically significant differences were demonstrated among the various aged groups ($p \leq 0.01$). The mean BMI was (32.70 ± 1.67) kg/m² for the (25–35) year group, same as that in the 36–45-year group (32.62 ± 2.86 kg/m²), and higher than that in the (46– 55) year age category (33.56 ± 2.86 kg/m²), according to Tables 1-1 and 1-2.

Table 1-1. Serum concentrations of Spexin, Nesfatin-1, Insulin, Glucose, HOMA-IR, and BMI in obese participants and controls. Data are presented as mean ± SD. Different letters indicate statistically significant differences at $p \leq 0.01$.

Variables	Patient (Mean ± SD)	Control (Mean ± SD)	p-value
Spexin	638.27 ± 58.12 b	860.33 ± 28.79 a	p ≤ 0.01
Nesfatin-1	195.65 ± 25.66 b	247.99 ± 36.93 a	p ≤ 0.01
Insulin	11.24 ± 1.36 a	6.80 ± 1.82 b	p ≤ 0.01
Glucose	186.73 ± 7.16 a	85.50 ± 2.99 b	p ≤ 0.01
HOMA IR	5.33 ± 1.07 a	1.42 ± 0.87 b	p ≤ 0.01
BMI	32.87 ± 2.44 a	23.36 ±1.74 b	p ≤ 0.01

Source: Own authorship.

Table 1-2. Serum concentrations of Spexin, Nesfatin-1, Insulin, Glucose, HOMA-IR, and BMI according to age groups in obese participants. Data are presented as mean ± SD. Different letters within each variable indicate statistically significant differences among age groups at $p \leq 0.01$.

Age group / Variables	Age (25–35) Mean ± SD	Age (36–45) Mean ± SD	Age (46–55) Mean ± SD
Spexin	668.36 ± 55.54 a	604.20 ± 61.47 a	642.25 ± 57.35 a
Nesfatin-1	201.39 ± 26.89 a	180.72 ± 21.19 a	204.84 ± 28.92 a
Insulin	12.38 ± 1.27 a	10.80 ± 1.22 a	10.56 ± 1.60 a
Glucose	169.03 ± 5.44 c	186.31 ± 6.08 b	204.86 ± 9.96 a
HOMA IR	3.01 ± 0.38 c	4.80 ± 0.45 b	5.20 ± 0.24 a
BMI	32.70 ± 1.67 a	32.62 ± 2.86 a	33.56 ± 2.86 a

Source: Own authorship.

Discussion

The purpose of the current study was to assess the changes in serum Spexin and Nesfatin-1 levels, and their correlation with insulin resistance and glucose metabolic dysfunction in Men with obesity, and also to investigate the impact of aging on these parameters. The principal findings demonstrated a marked decrease in Nesfatin-1 and Spexin and marked increased insulin levels in the patients with obesity when compared to healthy subjects. There were no statistical differences of these hormones in different age groups. There was, however, a clear progressive increase in fasting glucose and insulin resistance (HOMA-IR) with age in obese.

Nesfatin-1, Spexin, and Obesity

The apparent decrease on Nesfatin-1 levels in Men with obesity agrees with the established anorexigenic action of this peptide, as well as its impairment over glucose and lipids metabolism. This decrease could be due to a hypothalamic signaling deficiency or to inflammation-dependent variations in Nesfatin-1 secretion and regulation related to obesity. It has been reported that obesity disturbs hormonal balance in the control of appetite and energy homeostasis, and Nesfatin-1 may have an insulin-sensitising property as well as maintain glucose or lipid homeostasis, satiety regulations and therefore overall metabolic homeostasis **[14]**.

The expression of nesfatin-1 is found in several hypothalamic sites involved for energy intake and a broad range of other tissues, where it plays an important role in white adipose tissue inflammation modifications particularly in obesity-induced inflammation strikingly **[15]**. Likewise, reduction of spexin (SPX) in obese subjects was observed also in this investigation which is consistent with its known function as monitor of lipid and carbohydrate metabolism. Lower SPX is related to weight gain and energy imbalance, supporting the use of SPX as a biomarker of metabolic disorders associated with obesity **[16]**. These results provide new insight into SPX as an endocrine factor to regulate energy metabolism. The anti-obesity effect of SPX might be attributed to its anorexic actions, inhibition of lipid uptake and increase in insulin sensitivity and peripheral

action (adipose tissue, pancreas, and liver) as mentioned by **[17]**. Low levels of SPX were also observed in diabetic and obese patients (decreased SPX nearly 50%) in all ages, children/adolescents and adults, with a negative correlation to BMI parameters and insulin level in Turkey **[18]**. Taken together, these findings imply that changes in Nesfatin-1 and SPX are indicative of the presence of obesity per se, rather than age.

Insulin and Insulin Resistance

Insulin resistance (IR) is a leading public health problem due to its intimate correlation with metabolic syndromes, including obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM). IR is characterized by peripheral tissues being unable to effectively respond to insulin and hence it serves as a primary cause of disrupted glucose homeostasis **[19]**. It is the basis of T2DM, CVD, NAFLD, and MetS. In obese subjects, elevated IR is a risk factor for acute cardiovascular events such as myocardial infarction, leading to reduced glucose uptake and hyperglycemia **[20]**.

This study demonstrated that fat mass negatively affected serum insulin concentrations in hollow viscera and obesity increased their mixed serum insulin level, as a sign of compensatory hyperinsulinemia related to insulin resistance. These results are in line with there being no change **[21]** who observed hyperinsulinemia to be an early compensatory mechanism for high free fatty acids and metabolic dysregulation that occurs in the setting of obesity **[22]** similarly pointed out that obesity even in nondiabetic subjects affected insulin secretion dynamics. The higher fasting insulin level in obese individuals is therefore a result of the compensation mechanisms induced by obesity related IR, one of the main pathophysiological factors of this disorder **[23]**. Obesity leads to wide metabolic dysregulation including high fasting insulin and HOMA-IR. Interventions such as fasting and lifestyle changes have been reported to decrease fasting insulin level, improving insulin sensitivity in obese people along with improvements in the inflammatory status and metabolic variables **[24]**. Although insulin was found to be higher, there were no statistical differences between age groups, suggesting that compensatory hyperinsulinemia is primarily obesity driven and not influenced by the specific age among this range of ages.

Glucose, Insulin Resistance, and Aging

One of the main results in the present study was that fasting glucose levels and insulin resistance were significantly higher in Men with obesity with significant differences across age categories, suggesting a gradual increase with increasing age. This can be caused by aged diminished body lean mass, greater visceral fat accumulation and failure of the action of insulin, which together promote the progression of insulin resistance and glucose homeostasis disturbance. This trend is consistent with previous reports which emphasized a strong correlation between obesity, age and type 2 diabetes **[25]**. As a result of fasting glucose are mainly due to the enhancement in hepatic glucose production secondary to hepatic insulin resistance. This leads to insulin's inability to inhibit glycogenolysis and gluconeogenesis from non-gluconeogenic substrates like amino acids and fats. As a result, glucose is still released into the circulation during fasting and there are very high fasted glucose levels **[24-26]** suggested that insulin resistance and glucose dysregulation are a key in the pathogenesis of metabolic syndrome, particularly aging as age progresses even though diabetes was not overtly present.

Study Limitations

Despite the valuable insights provided by this study, certain limitations should be considered. The sample size was relatively small and limited to adult men from a single city, which may affect the generalizability of the findings. Additionally, the cross-sectional design prevents the establishment of causal relationships. Further longitudinal studies with larger and more diverse populations are recommended to validate and expand upon these findings.

Conclusion

The current study supports the following deductions:

1. Spexin and Nesfatin-1 are also found to decrease significantly in Men with obesity , which indicates their potential as predictive markers for T2D.
2. Obesity volunteers had significantly higher levels of fasting insulin, glucose, HOMA-IR, and BMI, which may lead to obesity known comorbidities like type 2 diabetes as it has been shown that insulin resistance plays a critical role as an underlying mechanism in the relationship between metabolic syndrome and hyperglycemia.
3. The relationship between BMI values and Spexin, and Nesfatin-1 was negatively correlated, in contrast the correlation with fasting glucose, insulin, and HOMA-IR was positive.
4. There were no significant effects of age on the measured hormonal markers except for fasting glucose, insulin, and HOMA-IR that increased with increasing age.

CRediT

Author contributions: Conceptualization, methodology, investigation, data collection, formal analysis, data interpretation, supervision, writing—original draft: All authors.

Acknowledgment

Not applicable.

Ethical Approval

The study protocol was reviewed and approved by the Scientific Research Ethics Committee of the Department of Biology, College of Education for Pure Sciences, University of Kirkuk (Approval Ref: BCPSKU/007/007H; Date: 5 August 2025). All research procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant international ethical guidelines. Written informed consent was obtained from all participants prior to their inclusion in the study, and confidentiality and privacy of participants' data were strictly maintained.

Informed Consent

Informed consent was obtained from all participants involved in the study, with all procedures explained in detail before participation.

Funding

Not applicable.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request, and all data is stored following privacy and ethical guidelines

Conflict of Interest

The authors declare no competing interests.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

References

1. Ahmed SK, Mohammed RA. Obesity: prevalence, causes, consequences, management, preventive strategies and future research directions. Metabolism Open. 2025;27:100375. doi: 10.1016/j.metop.2025.100375. Available from: https://doi.org/10.1016/j.metop.2025.100375.
2. Huang Q, Li Y, Yu M, Lv Z, Lu F, Xu N, Zhang Q, Shen J, Zhu J, Jiang H. Global burden and risk factors of type 2 diabetes mellitus from 1990 to 2021, with forecasts to 2050. Front Endocrinol. 2025;16:1538143. Available from: https://doi.org/10.3389/fendo.2025.1538143.
3. Blüher M. An overview of obesity-related complications: the epidemiological evidence linking body weight and other markers of obesity to adverse health outcomes. Diabetes Obes Metab. 2025;27 Suppl 2:3–19. Available from: https://doi.org/10.1111/dom.16263.
4. Wu Y, Li D, Vermund SH. Advantages and limitations of the body mass index (BMI) to assess adult obesity. Int J Environ Res Public Health. 2024;21(6):757. Available from: https://doi.org/10.3390/ijerph21060757.
5. Kosmas CE, Bousvarou MD, Kostara CE, Papakonstantinou EJ, Salamou E, Guzman E. Insulin resistance and cardiovascular disease. J Int Med Res.2023;51(3):3000605231164548.Availablefrom:https://doi.org/10.1177/03000605231164548.
6. Fang P, She Y, Yu M, Yan J, Yu X, Zhao J, Jin Y, Min W, Shang W, Zhang Z. Novel hypothalamic pathways for metabolic effects of spexin. Pharmacol Res. 2024;208:107399. Available from: https://doi.org/10.1016/j.phrs.2024.107399.
7. Aydemir İ, Yasul Y, Akbulut T, Cinar V, Migliaccio GM. Exercise-induced regulation of spexin: implications for metabolic health: a systematic review and meta-analysis. Medicina (Kaunas). 2026;62(1):107. Available from: https://doi.org/10.3390/medicina62010107.
8. Oh-I S, Shimizu H, Satoh T, Okada S, Adachi S, Inoue K, Eguchi H, Yamamoto M, Imaki T, Hashimoto K, Tsuchiya T, Monden T, Horiguchi K, Yamada M, Mori M. Identification of nesfatin-

1 as a satiety molecule in the hypothalamus. Nature. 2006;443(7112):709–712. Available from: https://doi.org/10.1038/nature05162.

9. Damian-Buda AC, Matei DM, Ciobanu L, Damian-Buda DZ, Pop RM, Buzoianu AD, Bocsan IC. Nesfatin-1: a novel diagnostic and prognostic biomarker in digestive diseases. Biomedicines. 2024;12(8):1913. Available from: https://doi.org/10.3390/biomedicines12081913.
10. Wojciechowska M, Kolodziejski PA, Pruszynska-Oszmalek E, Leciejewska N, Krauss H, Checinska-Maciejewska Z, Sassek M, Rekas-Dudziak A, Bernatek M, Skrzypski M, Wilczak M. Cord blood spexin level in mothers with obesity-forecast of future obesity?. Children (Basel). 2023;10(9):1517. Available from: https://doi.org/10.3390/children10091517.
11. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i–253.
12. Trinder P. Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J Clin Pathol. 1969;22(2):158–161. Available from: https://doi.org/10.1136/jcp.22.2.158.
13. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–1495. Available from: https://doi.org/10.2337/diacare.27.6.1487.
14. Mohammed Ali MJ. Assessment of leptin and nesfatin-1 with antioxidant capacity in obese Iraqi patients. Iraqi J Humanit Soc Sci Res. 2023;11:562–569.
15. Gharanei S, Ramanjaneya M, Patel AH, Patel V, Shabir K, Auld C, Karteris E, Kyrou I, Randeva HS. NUCB2/nesfatin-1 reduces obesogenic diet induced inflammation in mice subcutaneous white adipose tissue. Nutrients. 2022;14(7):1409. Available from: https://doi.org/10.3390/nu14071409.
16. Bufano A, Iraci Sareri G, Ciuoli C, Cantara S, Marzocchi C, Benenati N, Batzibal MS, Bombardieri A, Caprio S, Sannino I, Voglino C, Tirone A, Vuolo G, Dalmiglio C, Castagna MG. Normalization of spexin levels in patients with obesity submitted to bariatric surgery. Obes Surg. 2024;34(2):449–455. Available from: https://doi.org/10.1007/s11695-023-06972-x.
17. Sun L, Wang Z, Wang B, Jia Y, Zhao Q, Zhao J, Huang X. Body mass index impacts the lipid-lowing effects of statins in patients with type 2 diabetes. Front Cardiovasc Med. 2025;12:1493613. Available from: https://doi.org/10.3389/fcvm.2025.1493613.
18. Türkel İ, Memi G, Yazgan B. Impact of spexin on metabolic diseases and inflammation: an updated minireview. Exp Biol Med (Maywood). 2022;247(7):567– 573. Available from: https://doi.org/10.1177/15353702211072443.
19. Ballena-Caicedo J, Zuzunaga-Montoya FE, Loayza-Castro JA, Bustamante-Rodríguez JC, Vásquez Romero LEM, Tapia-Limonchi R, De Carrillo CIG, Vera-Ponce VJ. Global prevalence of insulin resistance in the adult population: a systematic review and meta-analysis. Front Endocrinol. 2025;16:1646258. Available from: https://doi.org/10.3389/fendo.2025.1646258.
20. Assani MZ, Boldeanu L, Dijmărescu AL, Caragea DC, Vladu IM, Clenciu D, Mitrea A, Stroe-Ionescu AȘ, Caragea ME, Siloși I, Boldeanu MV. Beyond HOMA-IR: comparative evaluation of insulin resistance and anthropometric indices across prediabetes and type 2 diabetes mellitus in metabolic syndrome patients. Life (Basel). 2025;15(12):1845. Available from: https://doi.org/10.3390/life15121845.
21. Fryk E, Olausson J, Mossberg K, Strindberg L, Schmelz M, Brogren H, Gan LM, Piazza S, Provenzani A, Becattini B, Lind L, Solinas G, Jansson PA. Hyperinsulinemia and insulin resistance in the obese may develop as part of a homeostatic response to elevated free fatty acids: a mechanistic case-control and a population-based cohort study. EBioMedicine. 2021;65:103264. Available from: https://doi.org/10.1016/j.ebiom.2021.103264.
22. Chiriacò M, Tricò D, Petrie JR, Gabriel R, Gastaldelli A, Nolan J, Lalic N, Mingrone G, Mari A, Natali A. Impact of overweight and obesity on fasting insulin secretion in men and women without diabetes: effect sizes and mechanisms. Diabetologia. 2025. Advance online publication. Available from: https://doi.org/10.1007/s00125-025-06643-9.
23. Gołacki J, Matuszek M, Matyjaszek-Matuszek B. Link between insulin resistance and obesity-from diagnosis to treatment. Diagnostics (Basel). 2022;12(7):1681. Available from: https://doi.org/10.3390/diagnostics12071681.
24. Lu L, Chen X, Liou S, Weng X. The effect of intermittent fasting on insulin resistance, lipid profile, and inflammation on metabolic syndrome: a GRADE assessed systematic review and meta-analysis. J Health Popul Nutr. 2025;44(1):293. Available from: https://doi.org/10.1186/s41043-025-01039-2.
25. Lin W, Rao H, Huang H, Yao J, Liang J, Li L, Wen J, Chen G. Relationship between insulin-

sensitive obesity and retinal microvascular abnormalities. Ann Palliat Med. 2021;10(2):1031–1041. Available from: https://doi.org/10.21037/apm-20-447.

26. Barroso E, Jurado-Aguilar J, Wahli W, Palomer X, Vázquez-Carrera M. Increased hepatic gluconeogenesis and type 2 diabetes mellitus. Trends Endocrinol Metab. 2024;35(12):1062–1077. Available from: https://doi.org/10.1016/j.tem.2024.05.006.