International Journal of Health Science & Biomedicine (IJHSB)
e-ISSN: 3139-3691

RESEARCH ARTICLE OPEN ACCESS

The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects

Nasreen Kader Kame

Kirkuk University, College of pharmacy, Kirkuk City-Iraq

Correspondence: Nasreen Kader Kame, Kirkuk University, College of pharmacy, Kirkuk City-Iraq, Email: nasreen@uokirkuk.edu.iq

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

Received Date: 2026-05-03, **Accepted Date:** 2026-05-17, **Published Date:** 2026-05-30

Keywords: Nesfatin-1; Fetuin-A; Obesity; InsulinResistance; GenderDifferences; Metabolic Syndrome; Sex Hormones; Inflammation.

Abstract

Background: Metabolic syndrome is significantly influenced by obesity. Hormonal dysregulation involving hepatokines and adipokines characterizes it. The interactions of fetuin-A, nesfatin-1, leptin, and adiponectin with sex hormones in obese and non-obese subject was examined in this study.

Methods: A total of 140 adults (70men and 70 women) were examined in this cross-sectional study. Fetuin-A, Nesfatin-1, leptin, adiponectin, lipid file, oxidative stress markers(MDA, GSH), inflammatory markers (CRP, IL-6, TNF-α), HbA1c,(Homeostatic Model Assessment for Insulin Resistance) HOMA-IR, testosterone, and estradiol status were all measured using blood samples. Group comparisons (obese men vs. obese women) were performed using t-tests, and associations were assessed using Pearson's correlation ($p < 0.05$).

Results: Obese men had an unfavorable metabolic profile compared to obese women with a statistically significant increase in blood pressure, triglycerides, LDL-c, HOMA-IR,HbA1c, CRP, IL-6,TNF-α, Fetuin-Aandleptin. The men had significantly lower levels of Nesfatin-1 and adiponectin compared with obese women and the correlation analysis exposed the damaging axis associated with leptin and fetuin serum levels and owing to insulin resistance with pro-inflammatory (CRP,IL-6) when oxidative stress markers at high MDA with low GSH. The result shows the leptin with Nesfatin-1 advancing to document the protective axis that supported insulin sensitivity after favorable lipid levels after increases the antioxidant substancessuch as GSH. Hormone testosterone has a highly positive correlation with the damaging axis (Fetuin-A: $r= 0.71$, $p < 0.001$)when indicating the potential role in the insulin resistance,while estradiol hormone has a low positive correlation with the protective axis (Nesfatin- 1: $r = 0.48$, $p = 0.004$).Conclusion: The pathophysiology associated with obesity can be defined in both males and females, through the injurious Leptin with Fetuin-A axis, through the protective Adiponectin with Nesfatin-1 axis. So, the data that resulted with this investigation provide catalogs for sex hormones may be important for determination the metabolic risk factors that may be important for determining the metabolic risk factors resulting from obesity through utilizing different biomarker hubs. Therefore, the study investigates that assessing sex hormone concentrations and biomarkers related to obesity provides useful information for developing and implementing tailored therapeutic interventions to regulate these pathways and improve metabolic health overall.

Introduction

The excess body fat is the major factor of obesity ,which according to the WHO that affected approximately 650 million people, or roughly 13 percent of the adult population worldwide as of 2023 [1]. In addition to the individual effects of obesity, it is important to understand that obesity is the major contributor to multiple metabolic syndrome disorders, which are characterized by various diseases including hypertension, dyslipidemia, insulin insensitivity and systemic chronic low-grade inflammation; each of which is linked to greater incidences of more serious chronic diseases, such as diabetic type II, cardiovascular disease and hepatic lipid accumulation [2]. Physiologically, obesity disrupts a delicate network of hormonal and metabolic signals. This disruption occurs through the intervention by the adipokines, such as leptin and adiponectin, and the hepatokines, such as fetuin-A [3]. It creates energy dysregulation and excessive storage of lipids in the adipocytes and consequently initiates a chronic inflammatory response. Such alterations induce the cycle of the imbalance and the dysfunction in the organism, and increased susceptibility to the chronic disease [4]. The metabolic syndrome in the obesity must be the risk factor that estimated at 20-25% in this study and the high blood pressure refers to consistently elevated diastolic and systolic pressures, which indicating through vascular events related to excessive adiposity. Dyslipidemia could be identified as highly elevated LDL cholesterol, triglycerides, and low HDL cholesterol, which promote a higher chance of developing atherosclerosis, leading to CV events. Insulin resistance may be demonstrated as impaired glucose uptake with added higher insulin concentrations, making the metabolic dysfunction more complex [5]. In addition, low-grade chronic inflammation accompanied by high levels of C-reactive protein (CRP) could result in continued tissue damage, leading to higher morbidity. The effects of obesity are compounded by each of the metabolic disorders noted above; thus resulting in an exponential increase in the extent of damage to one's health associated with each disorder [4]. Nesfatin-1 consist of 82-amino-acids ,which is produced from the nucleobindin-2 (NUCB2)

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.21009609

The mechanism of appetite suppression by nesfatin-1 occurs via modulation of hypothalamic melanocortin pathways, which directly influence the regulation of energy balance and body weight [6]. Nesfatin-1 was made in the hypothalamus and pancreatic cells, also stomach cells; it works in the body to stimulate pro-opiomelanocortin (POMC) nerve cells and simultaneously inhibit agouti- related peptide (AgRP) and neuropeptide Y (NPY) nerve cells [7]. These interventions appear to enhance beta-cell secretions from the pancreas while simultaneously improving glucose uptake/usage in muscle and adipose tissues. For nesfatin-1, as it relates to energy homeostasis, the importance of this continues to be evident. Based on this data, researchers have demonstrated that overweight subjects will exhibit substantially reduced plasma nesfatin-1 concentrations compared to those who maintain a normal weight. Overweight individuals will generally also experience a greater level of hunger and increased body weight, and ultimately exhibit negative metabolic effects associated with the increase in their body weight [8]. In addition to regulating energy homeostasis, nesfatin-1 also has an anti-inflammatory effect; it has been demonstrated that nesfatin-1 will inhibit pro-inflammatory cytokine production (i.e., interleukin 6 [IL-6] and tumor necrosis factor (TNF-α)), which are elevated in obesity, and are associated with elevated insulin resistance and an increased risk for cardiovascular disease [9]. On the other hand, fetuin-A is a major (64-kDa) glycoprotein produced mainly by the liver and plays a significant role in regulating metabolism associated with obesity [10, 11]. Fetuin-A could be intrinsic inhibitor for insulin receptor called tyrosine kinase, due to contributing to the insulin resistance, which has a major characteristic for both obesity and type 2 diabetes ,and high levels of fetuin-A have been shown to be closely correlated with visceral fat and therefore represent an additional cardiometabolic risk factor for developing cardiometabolic disorders [12]. This study aimed to examine the effect of Nesfatin-1 and Fetuin-A in terms of regulating the metabolism of a group of healthy, non-obese, and obese males. The study will also involve an examination of the effect of sex hormones (testosterone and estradiol) on these markers and the resulting metabolic patterns, based on the current literature, which are limited in sample sizes, methodology, and biochemical variables. This study aims to provide new avenues for approaches to the management of obesity and its associated complications, as well as to evaluate the combined effect of both markers on metabolic parameters such as the lipid profile, blood pressure, and inflammatory markers for the purpose of comparison with existing and emerging therapy options.

Methodology

Research Design

This cross sectional study was performed from January 2022 until December 2023 in Kirkuk General Hospital and private laboratories connected to Kirkuk General Hospital (KGH), in Iraq. The objective was to determine the effects of Fetuin-A, Nesfatin-1 and sex hormones on metabolism among obese, overweight and normal weight individuals of both genders. The reason for both KGH and private laboratories selected was to take advantage of the large and varied patient base as well as access to state-of-the-art diagnostic facilities. All participants consumed a defined diet (2000 - 2500 kilocalories of food per day, with 50% carbohydrates, 30% fats and 20% proteins) for a period of three days prior to their blood collection and performed their usual physical activity as measured by the validated questionnaire [12].

Ethical Considerations

The study followed the ethical principles for the Helsinki declaration was conducted following by the research and the permission of the research project was granted by the Kirkuk General Hospital Institutional Review Board (IRB approval number: KGH-2022-117) [13]. Research is conducted internationally with the intent to protect and provide for the welfare of the participants. All potential participants were given a written explanation in their primary language regarding the objectives of the research and methods used for conducting the research, and asked to provide informed consent. All data collected during the study were de-identified in order to protect the identity of all participants, and laboratory methods were performed in accordance with established protocol to ensure accurate results.

Sample Plan and Justification

This research used a stratified random sampling method to provide an unbiased representation of the Adults population studied from the Kirkuk Region ,and completed the questionnaire based on their health behaviors, when the sample was randomly selected from a population of adults aged 25 to 55 years visiting Kirkuk General Hospital for a regular check-up period, the sampling frame was adults visiting the hospital for routine check- ups. Once the population was determined, it was stratified by gender for upward balance (70 men, 70 women). Then, for each gender stratification, probable participants were stratified by their measured BMI into three categories: obese (BMI > 30 kg/m^2), overweight (25-29.9 kg/m^2), and non-obese (18.5-24.9 kg/m^2). Using computer-generated random numbers, a random number draw was generated for a pre-determined number of participants from each gender-BMI grouping, which resulted in a sample of 140 participants (70 obese adults, 35 men and35women), and(70 non-obese adults,35men and 35 women). The sampling strategy of using a stratified random selection is a probabilistic sampling strategy that collectively improves the external validity of the results because researchers can reduce selection bias and increase the likelihood of the sample being representative of the Kirkuk population that has similar health characteristics.

Participant Consent

All participants gave written informed consent before they took part in the research. The consent process included discussion face-to-face and written documentation in the local language outlining the goals and protocol of the research and participants' rights to withdraw without penalty. The only person who had access to participants' data was the lead investigator. The forms of consent were placed in a locked cabinet within the investigator's office.

Inclusion Criteria

Eligible participants were healthy, active adults aged 25-55 years, classified by BMI as obese, overweight, or non-obese, with fasting glucose <126 mg/dL, blood pressure <140/90 mmHg, and no medications for metabolic, lipid, or hormonal conditions. To provide the means for controlling the estradiol levels, the research inclusion of women in the follicular phase (days 1-14).

Exclusion Criteria

Exclusion criteria included individuals with a fasting glucose level greater than 126 mg/dL, those experiencing uncontrolled hypertension (pulse pressures of 160 mmHg and higher and/ or a diastolic pressure of 100 mmHg or higher), patients diagnosed with chronic disease(s) (e.g., diabetes, heart disease), and women taking medications that could affect metabolism. Any patient not in the follicular phase was excluded from the sample and rescheduled, this was necessary to eliminate confounding factors in the analysis of the total amount of estradiol in all the

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

participants so that it could be uniformly measured for the study. Any woman whose age or body mass index did not fall within the study's specified parameters was also excluded from the sample.

Sample Size

The participants consisted of 140 participants (70 men and 70 women), including 35 obese participants, 35 overweight participants, and 70 non-obese participants. For calculation the sample size was using power calculations (the effect size is 0.75, and power 85%, α=0.05)[12]. In order to achieve the statistical significance differences for lipid parameters ,Nesfatin-1 with Fetuin-A and sex hormones to allow the study's schedule with resources.

Data Collection Instruments

Fasting blood samples measured lipid profiles (total cholesterol, triglycerides, LDL-c, HDL-c), Nesfatin-1, Fetuin-A, CRP, HbA1c, HOMA-IR, IL-6, TNF-α, testosterone, and estradiol. ELISA quantified Nesfatin-1, Fetuin-A, IL-6, TNF-α, and CRP (R&D Systems). Twenty samples were taken for both gender(10 per each gender) were validated by using western blot and mass spectrometry (Orbit rap, Thermo Fisher Scientific). HbA1c used HPLC. HOMA-IR was estimated as (Fasting Insulin [μIU/mL] × Fasting Glucose [mmol/L])/22.5 [14],while the lipids were analyzed enzymatically and the HDL-c via direct assay ,but the LDL-c via Martin-Hopkins method [15]:LDL-c (mg/dL) = Non-HDL-C - (Triglycerides / Adjusted Factor),using a 180-cell stratification table. CRP used an automated analyzer. Height (audiometer), weight (calibrated scale), BMI, and blood pressure (sphygmomanometer) were measured. Smoking, alcohol, and activity were assessed via IPAQ.

Data Collection Process

Blood sample was taken at 8:00 AM to 10:00 AM in the morning after fasting overnight, when the participants followed the standardized diet and avoided strenuous exercise for 24 hours. The samples were taken in duplicate to ensure reliability for the application and centrifuged at 3000RPM for 10 minutes until serum was in a state of readiness, and samples were then either tested or promptly added to the 80 degrees Celsius freezer to ensure that the integrity of the biomarkers was preserved. Obesity was defined as BMI ≥30 kg/m² (WHO).

Enzyme-Linked Immunosorbent Assay (ELISA) Procedures

The Nesfatin-1, Fetuin-A, IL-6, TNF-α, and CRP concentrations were estimated commercially by using human sandwich available ELISA kits (DY056, DY516, D6050, DTA00D, DCRP00, R&D Systems, Minneapolis, MN) depending on the protocol kit. Each assay was based on a Sandwich ELISA design where samples and standards were added to antibody- pre-coated wells. After washing, a biotin-labelled detection antibody was added and followed by a streptavidin-HRP conjugate [16]. The colorimetric reaction was started by adding TMB substrate, which was stopped with acid that converted the blue solution to yellow. The optical density was estimation at 450nm and the intensity of color depend on the proportion to the concentration of the analyze, while the CVs were ≤8% (intra-assay) and ≤10% (inter-assay); detection limits: 0.1 ng/mL (Nesfatin-1), 2.0 ng/mL (Fetuin-A), 1.0 pg/mL (IL-6), 1.5 pg/mL (TNF-α),0.5 mg/L (CRP). Dilutions were re-analyzed as needed. Western blot (20 samples) used anti-Fetuin-A (1:1000, Abcam) and anti-Nesfatin-1 (1:500, Santa Cruz) antibodies (Fetuin-A: 64 kDa; Nesfatin-1: 9.7 kDa). Mass spectrometry confirmed identity (MASCOT >50).

Sex Hormone Assay

Serum total testosterone, estradiol, and cortisol concentrations were measured using commercially available specific chemiluminescent immunoassay (CLIA) kits on an automated analyzer (Abbott Architect i2000SR). All assays were done in duplicates according to the manufacturer's instructions [17]. Testosterone (0.08–17.00 nmol/L, CV <6%), estradiol (73–3420 pmol/L, CV <7%), and cortisol (27.6–1656 nmol/L, CV <5%) used duplicate assays. Women's samples were collected in the follicular phase, confirmed by cycle tracking.

Statistical Analysis

The statistical descriptive for measuring the blood pressure (BP), BMI, triglycerides, cholesterol, HOMA-IR, HbA1c, CRP, IL-6, TNF-α, Fetuin-A, Nesfatin-1, and sex hormones were calculated outcome. Independent t-tests were performed to compare mean variations among groups, with Cohen's d to calculate a measure of effect size. The correlation coefficients were calculated by using the Pearson correlation analysis significantly evaluations at the (P<0.05), While the multiple regression analysis was proceeding after alteration for the confounding factors (BMI, Age, cortisol, IL-6, CRP, TNF-α, and/or Lifestyle variables) and the analyses were performed utilizing only one method of statistical analysis software [18].

Data Availability

The data supporting the results of this research study can be made available upon request to the corresponding author, all requests must comply with ethical and privacy requirements. The raw data will remain securely stored at the Kirkuk General Hospital for at least five years, the summarized results will be made available with all appropriate precautions taken to protect confidentiality.

Results

Variations Between Groups in Metabolic Parameters

This study took place from January 2022 to December 2023 at Kirkuk General Hospital and nearby private laboratories in Iraq. Obese men had higher systolic blood pressure (SBP; 145.8 ± 13.9 mmHg vs. 140.2 ± 12.7 mmHg, t=2.45, P=0.017, Cohen's d=0.41) and diastolic blood pressure (DBP; 84.7 ± 5.0 mmHg vs. 81.3 ± 4.8 mmHg, t=3.01, P=0.004, Cohen's d=0.51) than women, suggesting the greater vascular strain in men. In terms of lipid profiles, men had greater triglycerides (128.6 ± 22.8 mg/dL vs. 118.4 ± 20.5 mg/dL, t=2.72, P=0.008, Cohen's d=0.46) but no significant differences were observed for total cholesterol (190.7 ± 18.2 mg/dL vs. 188.1 ± 17.6 mg/dL, t=0.87, P=0.389, Cohen's d=0.15), LDL-c, calculated using the Martin-Hopkins method, was also significantly higher in obese men (118.5± 14.2 mg/dL) compared to obese women (109.3 ± 13.1 mg/dL, t=2.85, P=0.006, Cohen's d=0.48), or HDL-c (27.1 ± 5.6 mg/dL vs. 28.9 ± 6.0 mg/dL, t=-1.33, P=0.188, Cohen's d=-0.22). CRP levels were also higher in men (16.8 ± 3.5 mg/L vs. 14.9 ± 3.2 mg/L, t=2.51, P=0.015, Cohen's d=0.43). Fetuin-A levels were higher in men (360.2 ± 28.7 ng/mL vs. 345.6± 27.3 ng/mL, t=2.28, P=0.026, Cohen's d=0.39), while Nesfatin-1 levels were lower in men (1.65 ± 0.35 ng/mL vs. 1.82 ± 0.38 ng/mL, t=-2.01, P=0.049, Cohen's d=-0.34). BMI was slightly higher in men (35.2 ± 3.4 kg/m² vs. 34.1 ± 3.2 kg/m², t=1.96, P=0.055, Cohen's d=0.33). There was no significant difference in age (40.1 ± 8.0 years vs. 39.4 ± 7.8 years, t=0.37, P=0.714, Cohen's d=0.06 [Table 1, Figure 1].

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

Parameter	Obese	Men	Men	Obese Women	Obese Women	t-	P-	Cohen'sd(95 %CI)
(n=35)	(n=35)	Mean	±	(n=35) Mean	±	value	value	value
	SD	SD	SD	SD				
SBP (mmHg)	145.8±13.9	145.8±13.9	140.2±12.7	140.2±12.7	2.45	2.45	0.017	0.41(0.07,0.75)
DBP (mmHg)	84.7± 5.0	84.7± 5.0	81.3± 4.8	81.3± 4.8	3.01	3.01	0.004	0.51(0.16,0.86)
Total	190.7±18.2	190.7±18.2	188.1±17.6	188.1±17.6	0.87	0.87	0.389	0.15(-0.19,0.49)
Cholesterol (mg/dL)								
TG(mg/dL)	128.6±22.8	128.6±22.8	118.4±20.5	118.4±20.5	2.72	2.72	0.008	0.46(0.12,0.80)
LDL-c(mg/dL)	118.5±14.2	118.5±14.2	109.3±13.1	109.3±13.1	2.85	2.85	0.006	0.48(0.14,0.82)
HDL-c(mg/dL)	27.1± 5.6	27.1± 5.6	28.9± 6.0	28.9± 6.0	-1.33	-1.33	0.188	-0.22(-0.56,0.12)
CRP(mg/L)	16.8± 3.5	16.8± 3.5	14.9± 3.2	14.9± 3.2	2.51	2.51	0.015	0.43(0.09,0.77)
IL-6(pg/mL)	5.1±1.2	5.1±1.2	4.3±1.0	4.3±1.0	2.38	2.38	0.02	0.40(0.06,0.74)
TNF-α(pg/mL)	3.9±0.8	3.9±0.8	3.2±0.7	3.2±0.7	2.67	2.67	0.01	0.45(0.11,0.79)
HbA1c(%)	6.8±0.9	6.8±0.9	6.3±0.8	6.3±0.8	2.1	2.1	0.04	0.35(0.01,0.69)
HOMA-IR	4.2±1.1	4.2±1.1	3.6±0.9	3.6±0.9	2.25	2.25	0.03	0.38(0.04,0.72)
Fetuin-A	360.2±28.7	360.2±28.7	345.6±27.3	345.6±27.3	2.28	2.28	0.026	0.39(0.05,0.73)
(ng/mL)								
Nesfatin-1	1.65±0.35	1.65±0.35	1.82±0.38	1.82±0.38	-2.01	-2.01	0.049	-0.34(-0.68,0.00)
(ng/mL)								
BMI(kg/m²)	35.2± 3.4	35.2± 3.4	34.1± 3.2	34.1± 3.2	1.96	1.96	0.055	0.33(-0.01,0.67)
Age(years)	40.1± 8.0	40.1± 8.0	39.4± 7.8	39.4± 7.8	0.37	0.37	0.714	0.06(-0.28,0.40)

Table 1: Metabolic Parameters in Obese Males and Obese Females

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

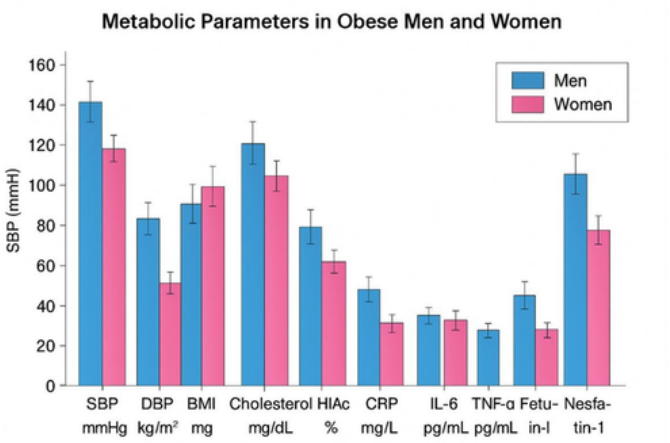

Figure 1: Comparative Analysis of Metabolic Parameters in Obese Males and Obese Females.

Correlation Tests of Obese Males and Obese Females

Strong positive relationships were remarked between Body Mass Index (BMI) and several metabolic variables in males. Specifically, BMI had strong positive relationships with systolic and diastolic blood pressure (SBP: r=0.75, p<0.001; DBP: r=0.62, p<0.001), triglycerides (r=0.68, p<0.001), LDL-cholesterol (r=0.60, p<0.001), a combination of inflammatory markers CRP, IL-6, and TNF-a (r=0.48, p=0.003; r=0.45, p=0.007; r=0.42, p=0.011 respectively), glycemic indices HbA1c and HOMA-IR (r=0.50, p=0.002; r=0.55, p<0.001), and the hepatokine Fetuin-A (r=0.72, p<0.001). A moderate negative relationship was found in HDL-cholesterol (r=-0.40, p=0.017), and no statistically meaningful correlations were found with Nesfatin-1 or total cholesterol levels.

A similar analysis in females showed comparable results; the BMI was positively related to all of the same parameters—blood pressure, lipids (excluding HDL-c), inflammatory markers, glycemic controls, and Fetuin-A—with the correlation coefficients and significance shown in [Table 2]. Again, and similarly to men, there was a negative correlation with HDL-(r=-0.38, p = 0.024), and there were no practically useful correlations with Nesfatin-1 or total cholesterol [Figure 2].

Parameter	Men(r)	MenP-value	Women(r)	WomenP-value
SBP(mm Hg)	0.75	<0.001	0.7	<0.001
DBP(mm Hg)	0.62	<0.001	0.58	<0.001
TotalCholesterol(m	0.09	0.602	0.07	0.689
TG(mg/dL)	0.68	<0.001	0.65	<0.001
LDL-c(mg/dL)	0.6	<0.001	0.57	<0.001
HDL-c(mg/dL)	-0.4	0.017	-0.38	0.024
CRP(mg/L)	0.48	0.003	0.45	0.007
IL-6(pg/mL)	0.45	0.007	0.42	0.012
TNF-α(pg/mL)	0.42	0.011	0.39	0.021
HbA1c(%)	0.5	0.002	0.47	0.004
HOMA-IR	0.55	<0.001	0.52	0.001
Fetuin-A(ng/mL)	0.72	<0.001	0.68	<0.001
Nesfatin-1(ng/mL)	0.1	0.565	0.08	0.645

Table 2: Pearson Relationships between BMI and Metabolic Factors in Obese Women and Men

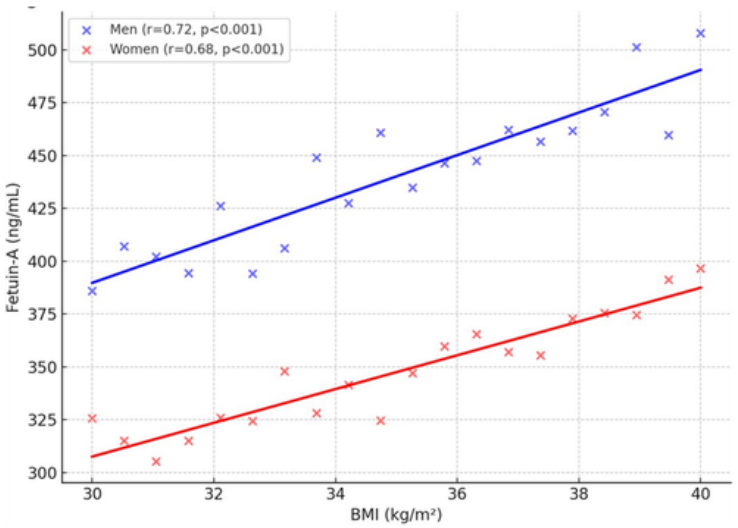

Figure 2: Relationship between BMI and Fetuin-A for Obese Men and Obese Women SBP-Related

Across the metabolic landscape, SBP emerged as a connective node with strong associations across the metabolic network. In men, high SBP was significantly related to other high values of DBP, triglycerides, LDL-c, CRP, IL-6, TNF-α, Haemoglobin A1C (HbA1c), Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), fetuin-A, and body mass index (BMI) (all p<0.05), as shown in [Table 3][Figure 3]. In compartment, SBP was negatively correlated with high-density lipoprotein cholesterol (HDL-c) and Nesfatin-1 levels.

Parameter	Men(r)	MenP-value	Women(r)	WomenP-value
DBP(mmHg)	0.82	<0.001	0.79	<0.001
TotalCholesterol(mg/d	0.11	0.53	0.09	0.605
TG(mg/dL)	0.71	<0.001	0.67	<0.001
LDL-c(mg/dL)	0.72	<0.001	0.68	<0.001
HDL-c(mg/dL)	-0.37	0.029	-0.35	0.039
CRP(mg/L)	0.45	0.007	0.42	0.012
IL-6(pg/mL)	0.43	0.01	0.4	0.018

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

TNF-α(pg/mL)	0.4	0.017	0.37	0.029
HbA1c(%)	0.48	0.004	0.45	0.006
HOMA-IR	0.53	<0.001	0.5	0.002
Fetuin-A(ng/mL)	0.69	<0.001	0.65	<0.001
Nesfatin-1(ng/mL)	-0.42	0.012	-0.39	0.021
BMI(kg/m²)	0.75	<0.001	0.7	<0.001

Table 3: Correlation Coefficients by Pearson of SBP and the Metabolic Parameters among Obese Men and Women Correlations

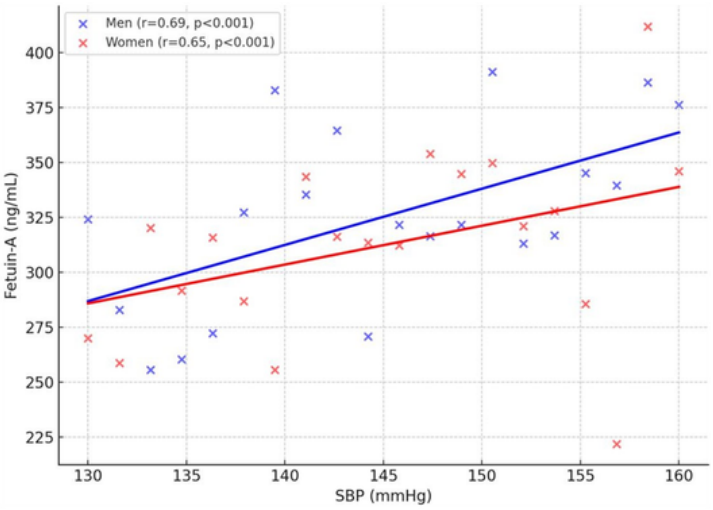

Figure 3: Correlation between SBP and Fetuin-A in Obese Men and Women Peptide-Specific Correlations

A mostly equivalent correlation pattern was also observed in women, with SBP positively correlated to the same adverse metabolic risk factors and negatively correlated with HDL-c and Nesfatin-1. The relationships in women were slightly weaker than those reported for men, but remained statistically significant, demonstrating a consistent relationship between higher blood pressures and broader variation in metabolic dysfunction. There was no involvement of total cholesterol with SBP in either sex.

Direct analysis of the biomarkers indicated differential associations. Fetuin-A concentration had a significant positive association with central inflammatory cytokines CRP [Figure 4], IL-6, and TNF-α in both male and female subjects, confirming its prospective role in inflammation. In contrast, in males, Nesfatin-1 had a significant negative association with LDL-cholesterol [Figure 5]. The was positive association intriguing result in women was suggested the possible interaction of gender roles in lipid metabolism with Nesfatin-1 concentrations that warrants further investigation.

Fetuin-A and Nesfatin-1 measurements were confirmed using Western blot and mass spectrometry in all 20 samples. The representative Western blot images showed the expected bands corresponding to the molecular weight of Fetuin-A (64 kDa) and Nesfatin-1 (9.7 kDa). Mass spectrometry confirmed peptide identity with an NIH-P33 and MASCOT score >50; appropriate standard errors (SEs) are used in [Tables 4-6].

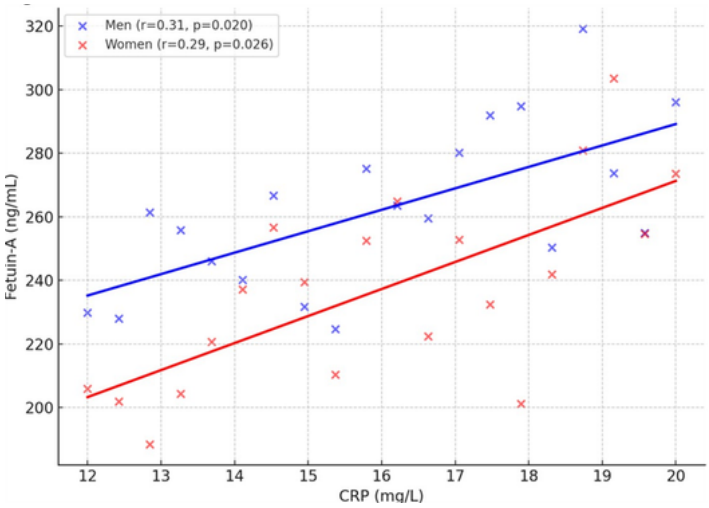

Figure 4: Correlation Between Fetuin-A and CRP in Obese men and women

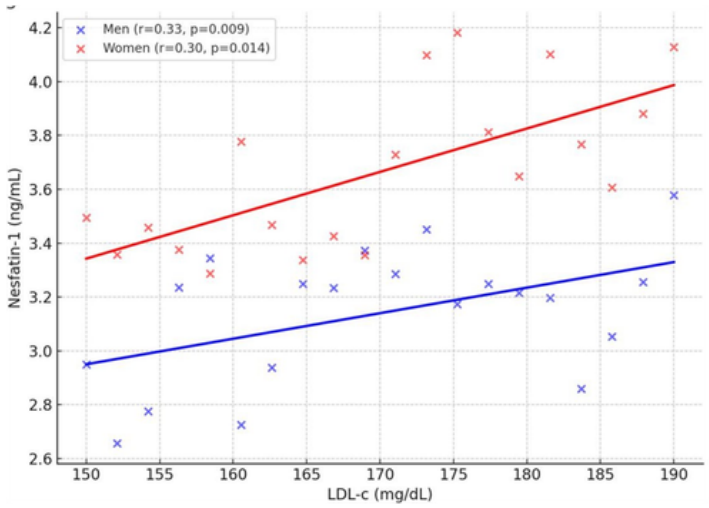

Figure 5: Correlation between Nesfatin-1 and LDL-c in Obese Men and Women Measurement Precision

Parameter	MenMean	MenSE	WomenMean	WomenSE
Nesfatin-1(ng/mL)	1.65	0.059	1.82	0.064
Fetuin-A(ng/mL)	360.2	4.85	345.6	4.61
CRP(mg/L)	16.8	0.591	14.9	0.541
IL-6(pg/mL)	5.1	0.203	4.3	0.169
TNF-α(pg/mL)	3.9	0.135	3.2	0.118
LDL-c(mg/dL)	118.5	2.72	109.3	2.6

Table 4: Standard Errors and Mean Values for Metabolic Parameters in Obese Women and Obese Men

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

HDL-c(mg/dL)	27.1	0.95	28.9	1.01
TG(mg/dL)	128.6	3.85	118.4	3.46
SBP(mmHg)	145.8	2.35	140.2	2.15
DBP(mmHg)	84.7	0.845	81.3	0.811
BMI(kg/m²)	35.2	0.574	34.1	0.541
HbA1c(%)	6.8	0.152	6.3	0.135
HOMA-IR	4.2	0.186	3.6	0.152

Table 5: Standard Error for Lipid Parameters, Nesfatin-1, and Glycemic Markers

Parameter	MenSE	WomenSE
LDL-c(mg/dL)	2.72	2.6
HDL-c(mg/dL)	0.95	1.01
TG(mg/dL)	3.85	3.46
TotalCholesterol(mg/dL)	3.08	2.97
Nesfatin-1(ng/mL)	0.059	0.064
HbA1c(%)	0.152	0.135
HOMA-IR	0.186	0.152

Table 6: Standard Error for CRP, IL-6, TNF-α, BMI, SBP, DBP, and Fetuin-A

Sex Hormonal Concentration and Effects on Metabolism in Obese Individuals

[Table 7], summarizes the differences in directly assessed testosterone, estradiol, and cortisol levels between the obese male and female participants.

Given the higher testosterone production in obese men than in obese women, it is reasonable that the circulating testosterone levels were significantly higher for men (12.8 ± 3.5 nmol/L) than women (1.6 ± 0.5 nmol/L; p< 0.001, Cohen's d = 3.21). Conversely, given the higher estradiol production by obese women than obese men, it is not surprising that the circulating estradiol levels were significantly greater for women (325.4 ± 85.1 pmol/L) than men (105.3 ± 30.2 pmol/L; p < 0.001, Cohen's d = 2.45). There were no differences in circulating cortisol levels between groups (M: 538 ± 95 nmol/L vs. F: 515 ± 88 nmol/L; p = 0.285).

Parameter	MenSE	WomenSE
CRP(mg/L)	0.591	0.541
IL-6(pg/mL)	0.203	0.169
TNF-α(pg/mL)	0.135	0.118
BMI(kg/m²)	0.574	0.541
SBP(mmHg)	2.35	2.15
DBP(mmHg)	0.845	0.811
Fetuin-A(ng/mL)	4.85	4.61

Table 7: Assessed Sex Hormone Concentrations and Associations with Important Biomarkers in Obese Individuals

Integration of Adipokine Pathways and Oxidative Stress

While hepatokines are involved in some aspects of the metabolism associated with obesity, adipokines are major contributors to the disruption of normal metabolism in obesity. Our analysis in [Table 8], indicates that some indicators of the alteration of normal metabolism have strong correlations with leptin levels, including the following: BMI (r = 0.82, p < 0.001), HOMA-IR (r = 0.75, p = 0.003), and Fetuin-A (r = 0.65, p = 0.018). The relationship between grade related hyperleptinemia and increased Fetuin-A synergistically to exacerbate the insulin resistance. Leptin correlated inversely and significantly with Nesfatin-1, the anorexigenic peptide (r=-0.55, p=0.045), which indicates a counterregulatory relationship with Nesfatin-1 suppressing the appetite inhibition effects of Leptin, and of course, Nesfatin-1 might have other potentially protective effects related to prepandial oxidative stress.

DependentV	**Independent**	**r-value**	**t-value**	**P-value**	**SE**	**SEM**
Leptin	BMI	0.82	6.91	<0.001	0.12	0.06
	HOMA-IR	0.75	5.72	0.003	0.13	0.07
	Fetuin-A	0.65	4.45	0.018	0.15	0.08
	Nesfatin-1	-0.55	-3.45	0.045	0.16	0.08
Adiponectin	BMI	-0.78	-6.12	0.002	0.13	0.07
	HDL-c	0.85	7.52	<0.001	0.11	0.06
	HOMA-IR	-0.8	-6.67	0.001	0.12	0.06
	Leptin	-0.76	-5.95	0.005	0.13	0.07

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

MDA	BMI	0.84	7.15	<0.001	0.12	0.06
	CRP	0.72	5.25	0.007	0.14	0.07
	Fetuin-A	0.69	4.82	0.01	0.14	0.07
GSH	BMI	-0.83	-6.81	<0.001	0.12	0.06
	Nesfatin-1	0.62	4.1	0.025	0.15	0.08
	MDA	-0.86	-7.75	<0.001	0.11	0.06

Table 8: Associations of Leptin and Adiponectin with Metabolic, Inflammatory, and Oxidative Stress Markers in the Obese Cohort (n=70)

Abbreviations: SE, Standard Error; SEM, Standard Error of the Mean; MDA, Malondialdehyde; GSH, Glutathione.

Discussion

This result provide a new hub for understand the significant marker for both gender at obesity condition that related the metabolic health. Earlier studies have always reported that men with obesity have much worse outcomes than women, yet this study signaling about how sex hormones and other biological factors are involved in the process of how obesity affects health differently based on one's sex. The result demonstrate that obesity does not have the same type of pathophysiology for every person; rather, obesity follows different channels determined by sex: when the men have an increased risk due to the adverse effects of a Fetuin-A with Leptin hormonal axis enhanced by testosterone, while the women have a decreased risk due to a protective Nesfatin-1and Adiponectin hormonal axis enhanced by estrogen. The [Table 1], illustrate notable gender differences in the metabolic with clinical characteristics profiles of obese subjects. These results were supported by Ramírez-Vélez et al. [18] that demonstrated the visceral fat accumulation in obese men,that increased the sympathetic nerve activations, which further impairs the function of blood vessels and sodium retention disorder and increasing the blood pressure. Men's higher visceral fat likely activates the renin-angiotensin-aldosterone system (RAAS), exacerbating hypertension [19]. Compared to earlier studies like Rashid et al. [20], which reported higher SBP (~150 mmHg) and DBP (~88 mmHg) in obese males, This results are somewhat lower. This difference may arise from variations in population characteristics, like geographic or genetic factors specific to the Iraqi group, and differences in measurement methods, including our standardized protocols.

The lipid profile assessment in [Table 1] and [Figure 1], shows that obese males had significantly higher triglyceride levels, which is a known indicator of insulin resistance and a major risk factor for atherosclerotic artery disease. This aligns with findings from Link and Reue [21], who linked elevated triglycerides in obese males to increased production of very- low-density lipoprotein (VLDL) in the liver, influenced by lower estrogen levels that usually help lipid clearance in females. In contrast, no significant differences were found in total cholesterol, LDL-cholesterol, or HDL-cholesterol. Results obtained by Milyani and Al-Agha [22] indicate that men had a lower mean HDL-cholesterol than women, ~25 mg/dL and ~30 mg/dL, respectively, possibly owing to the more lenient criteria used to include people with chronic conditions. Triglycerides appear to be a more sensitive gender-specific lipid marker, with estrogen promoting HDL synthesis and reducing VLDL in women [23]. Pro-inflammatory systemic inflammation was marked with elevated C-reactive protein (CRP) in obese males, as shown in [Table 1]. This supports the observations of Lee and Kim [24], who connected higher CRP levels in obese males to the inflammation caused by excess fat, which increases the risk of heart disease. In this study, the CRP values were consistent with the findings in obese individuals offered by Rumińska et al. [25] in average CRP levels for men- and women-only groups, which offered insight into the gender-based inflammatory load. Small BMI differences suggest metabolic variations stem from sex-specific physiological responses, particularly visceral fat in men and estrogen-modulated inflammation in women [26]. The circulating concentrations of Fetuin-A and Nesfatin-1 evaluated in this study supported the ranges reported in the existing literature. Zhou and colleagues found similar values of Fetuin-A reports in former studies of obese individuals, again, a similar trend of higher Fetuin-A values in males [27]. Similarly, the circulating concentrations of Nesfatin-1 reported here in [Figure 5], were within the range of values reported by Luo et al. [28] for obese populations. The correlation strengths in [Figure 4], that we found with CRP were slightly lower than the values found by Khadir et al. [3], demonstrate that there were some differences in metabolic markers, possibly due to the sample cohort differences. This small difference could be explained by differences in the demographic profile of the study population or technical differences in the immunoassays. This association between Fetuin-A levels and hepatic steatosis as shown by Peter et al. [29] further highlights its important role in insulin resistance and inflammatory processes, especially in men. The lower amounts of Nesfatin-1 seen in the obese males correspond with its known effects on both stimulation of appetite and glucose homeostasis [28]. Its inverse relationship with SBP [Table 3], indicates potential protective effects on vascular health, which aligns with findings from Lu et al. [30], who suggested that Nesfatin-1 may affect sympathetic nervous system activity and renal sodium activation by RAAS (r=-0.40 to -0.45 for SBP). The novel positive correlation with LDL-c [Figure 4], contrasts with weaker associations in Luo et al. [28] (r=0.20–0.25), suggesting a gender-specific lipid regulatory role needing further study. This might demonstrate either a compensatory mechanism in lipid metabolism or a different effect of Nesfatin-1 that warrants further assessment. Moreover, Nesfatin-1 was not correlated with BMI [Table 2], which is not consistent with Lopez-Aguilar et al. [31] (r=0.15-0.20). This suggests that Nesfatin-1 may play a predominantly regulatory role in vascular and lipid regulation and has no direct role in body weight. The reliability of our biochemical and clinical evedence was reflected in the low standard errors seen in [Tables 4-6]. Fetuin-A and Nesfatin-1 showed minimal variability similar to Zhou et al. [27] (Fetuin-A SE: ~4.5-5.0; Nesfatin-1 SE: ~0.05-0.07). Larger Fetuin-A SE in men may reflect variations in liver function or inflammation [3]. Lipoprotein profiles and blood pressure records showed homogeneous SEs comparable to the recommended clinical norms [19]. The similar BMI SEs (0.574 vs. 0.541) indicate accurate body measurements, which corroborates the work by Rumińska et al. [25]. The differences between Fetuin-A and Nesfatin-1 across sexes may have implications for their ability to act as biomarkers for obesity-related outcomes. The elevated levels of Fetuin- A in men suggest a greater risk for insulin resistance and cardiovascular diseases. Pan et al. [32] concluded that increased levels of Fetuin-A are associated with a two-fold increase in developing type 2

diabetes. The low levels of Nesfatin-1 found in males could play a role in appetite control and lipid metabolism. Luo et al. [28] identified Nesfatin-1 as a promising candidate for therapeutic interventions focused on appetite regulation. This results show the significant relationships pointing to a direct mechanistic role of Fetuin-A and associated peptides in the development of metabolic syndrome components ,when substantial gender differences in the metabolic phenotype of obesity .The elevated levels and strong positive correlations of Fetuin-A with BMI, the inflammatory markers measured in this study (CRP, IL-6, TNF-α), blood pressure, and HOMA-IR, respectively, provide a strong basis for Fetuin-A to be viewed as an overall pro-inflammatory and pro- diabetogenic mediator in obese men, where it inhibits the insulin receptor known tyrosine kinase and is elevated in hepatic steatosis [29]. The strong association with inflammation indicates that elevated Fetuin-A, likely from visceral adipose tissue release, also associated with pro-inflammatory cytokines released from adipose tissue, which could correlated with further increases in Fetuin-A, and therefore, a vicious cycle of deterioration. The observed elevations of Fetuin-A in men may also be accounted for by some measure of androgen regulation, as testosterone has been suggested to correlate with visceral adiposity and hepatic lipo genesis, key stimulators of Fetuin-A secretion [33].

In contrast, lower circulating levels of Nesfatin-1 in obese men suggest a potential protective effect of this peptide that is decreased in obesity. A reduction of Nesfatin-1 may have direct metabolic effects. Its strong and significant negative relationship with systolic blood pressure implies that decreased Nesfatin-1 may permit more vascular tone and hypertension, perhaps through actions on the sympathetic nervous system or on modifies functions of the endothelium. The relationship with LDL-cholesterol is curious and complicated, and is negative in men but positive in women. This should be investigated further, but it suggests Nesfatin-1 may interact with specific gender-associated characteristics, such as sex hormones, regarding their influence on lipid metabolism. Since Nesfatin-1's primary role is in central appetite suppression, a reduction in Nesfatin-1 would directly contribute to hyperphagia and subsequent weight gain, thereby perpetuating obesity. Higher levels of Nesfatin-1 in pre-menopausal women may be due to the protective effects of estrogen and, therefore, may investigated the partial explanation of the gender variations, which needed to be determined by direct measurements of hormones. Milyani & Al-Agha [22] identified triglycerides as a necessary consideration regarding fat metabolism conditions between genders. Targeted efforts to reduce Fetuin-A or enhance levels of Nesfatin-1 through diet may be strategies to reduce obesity-related health risks [26]. From a physiological and hormonal standpoint, our direct measurements provide a correlation link to explain the observed gender binary morphosim in metabolic parameters. The significantly higher levels of testosterone in obese men, coupled with the strong positive correlation between testosterone and Fetuin-A, strongly suggest that androgen excess is a key driver of the adverse metabolic profile. In men, testosterone levels and their relationship to Fetuin-A associated with visceral adiposity and hepatic lipo genesis, resulting in worsened insulin resistance and inflammation [34]. In women, estradiol showed a correlation with Nesfatin-1 ($r=0.48$, $p=0.004$), which improves endothelial function and lipid metabolism [35]. To better manage the menstrual cycle phase with respect to concentrations of estrogen, women were tested during the follicular phase (days 1-14) of the menstrual cycle when estradiol concentration peaks to ensure low variability and enhance reliability of the measures [36, 37]. This standardization would likely enhance the protective effects of estradiol on the activity of Nesfatin-1 and lipoprotein profiles. While cortisol levels did not differ significantly between groups, its weak correlation with Fetuin-A suggests a potential minor role in modulating metabolic inflammation. The differences in hormones suggest sexual dimorphism with respect to the relationships with Fetuin-A concentration, with testosterone amplifying the negative properties of Fetuin-A and estradiol amplifying the protective properties of Nesfatin-1, further suggesting a need for gender-specific interventions for obesity [38-40]. The impact of hormones on the sex-specific adipokine and oxidative stress pathways observed in this study is consistent with, and supports, the current literature. Moreover, the predominant cluster of inflammation and oxidative stress associated with high levels of leptin, Fetuin-A, and MDA is more pronounced in obese males. This finding supports the results of Tchernof and Després [19], who noted that the androgenic profile of men favors the accumulation of visceral fat and the production of hepatic triglycerides, inducing to the development of an excess of pathogenic adipokines and hepatokines in the body. This mechanistic pathway linking testosterone to a pro-inflammatory metabolic phenotype is a biochemical explanation for the well-established clinical observation of greater cardiometabolic risk in obese men.

Conversely, the protective cluster that consisted of higher adiponectin and Nesfatin-1 was greater in women, which remained potent owing to estradiol. These results agreement with Morán-Costoya et al. [41], who indicated that estrogen plays an important role in increasing the sustained secretion of adiponectin to promote insulin sensitivity and improve lipid metrics. This hormonal potentiation likely contributes to the meliorated antioxidant defense in women, and demonstrated through the strong inverse correlation between GSH and MDA, and this finding was more favorable metabolic environment that minimize the most serious consequence of obesity. To summarize the result, we propose the unified model for the pathophysiology of obesity, when posits the detrimental axis and the protective axis between both two key axes of estrogen with testosterone, and sex hormone-binding globulin (SHBG). This model extends the current paradigm of sex differences in metabolic disease. The axis when damaging was characterized by Leptin and Fetuin-A, which was acting in concert to drive inflammation with insulin resistance and oxidative stress, for exists on a spectrum that is greater in men. The protective axis is characterized by Adiponectin and Nesfatin-1, which act to support insulin sensitivity, promote lipid metabolism, and antioxidant capacity, and can be observed along a spectrum that is greater in women. Future forinterventions designed must be promote the restoration for metabolic homeostasis may enhance by greater specificity for acceptance in either men or women biological differences, such as considering Leptin to Fetuin-1 suppression in males or Adiponectin with Nesfatin-1 intervention in females, rather than just classical obesity therapies targeting weight management.

Conclusions

The present study augmentedto exist the evidence of substantial sexual dimorphism in the various metabolic indicators of obesity and governed by different biomarker axes with sex hormones operating as modulators. We identified and characterized two main axes: the pestilent Leptin to Fetuin-A axis, which quickens inflammation, insulin resistance, and oxidative stress that is supported by elevated testosterone levels in men, and the preventative Adiponectin to Nesfatin-1 hubs that advances insulin sensitivity, lipid metabolism, and antioxidant capacity that is augmented by estradiol in women.

Direct measures of testosterone and estradiol, accounting for the phase of menstrual status, underscored their importance to body composition and metabolic risk. Specifically, testosterone strongly correlated with the pro-inflammatory Fetuin-A biomarker, whilst estradiol was associated with the contingent anti-inflammatory

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

index biomarker Nesfatin-1. Further inclusion of markers of oxidative stress confirmed that the protective axis was associated with measures of lipid peroxidation (lower MDA) and antioxidant defence (higher GSH) factors that lowered metabolic risk.

These result assisted to explain the disorder cardio metabolic mechanism occur in the men with obesity than in obesity women. Since these two biomarker axes are expressed differentially by sex, they are rational targets for developing individualized obesity therapies. Fetuin-A and leptin could be considered when developing obesity interventions in men, while attempts to stimulate adiponectin and Nesfatin-1 effects may have more effect in women when it comes to developing interventions for obesity. Future multi-ethnic longitudinal studies and clinical trials are needed to establish the global applicability of this model and to test interventions targeting the deleterious axis and enhancing the protective axis as a way of preventing the underlying metabolic and inflammatory dysregulations of obesity-related weight gain, rather than just focusing on weight loss.

Justification for the Research

Obesity represents a significant global health concern, with metabolic syndrome serving as a primary mechanism influenced by dysregulated peptides such as Fetuin-A and Nesfatin-1. Prior research has reported a relationship between Fetuin-A and Nesfatin-1 and their association with appetite, insulin resistance, and inflammation. The major drawback of these studies was that they almost exclusively used small sample sizes and limited the type of Biomarker analysis performed.

This study intends to overcome these issues by investigating the major characteristics of Fetuin-A and Nesfatin-1, as well as their interaction with sex hormones for markers of Metabolic health, including blood pressure, Lipids and C-reactive protein, in a population of 70 Obese subjects, equally balanced between men (n=35) and women (n=35), using advanced statistical techniques to assess gender-based differences and hormone-based differences in Obesity Dysfunction. The study aims to clarify the physiological dysfunction caused by Obesity and serves as a basis for developing targeted therapy for patients, while also providing greater insight into Fetuin-A and Nesfatin-1's roles as Metabolic Biomarkers associated with Obesity.

Outcome of the Study

This objective provides the distinguished evidence for the effect of sex in obesity-related metabolic differences. For example, obese males exhibit many higher risk characteristics when compared to obese females, including elevated blood pressure (BP), triglycerides, systemic inflammatory markers (CRP, IL-6, TNF-α), HOMA-IR, HbA1c, and the biomarkers, Fetuin-A (increased) and Nesfatin-1 (decreased), as seen in [Table 1].

Additionally, correlation analyses provided additional mechanistic insight as high levels of Fetuin-A highly positively correlated with BMI and inflammatory markers. This supports the established relationship between Fetuin-A and both obesity and systemic inflammation, and the strong correlation with SBP suggests that Fetuin-A may be involved in OB-related hypertension. Conversely, Nesfatin-1 was inversely related to SBP, suggesting it may confer some protection on the vascular endothelium; however, there was a complex, gender-specific relationship between Nesfatin-1 and LDL-c levels. Furthermore, when incorporating age, BMI, and lifestyle activities into the multivariable regression analyses, both Fetuin-A and Nesfatin-1 remain independent predictors of adverse metabolic outcomes, further highlighting their potential utility as biomarkers to identify the pathophysiological mechanisms associated with obesity.

Constraints of the Research

The cross-sectional design precludes causal conclusions, and the temporal relationship of the metabolic change is undefined. Even though a stratified random sampling technique improves the internal validity and reduces selection bias, the generalizability of our results may have limitations driven by geographic and ethnic characteristics. The focus on Iraqi adults may restrict the generalizability of findings since hereditary and environmental influences vary among populations (e.g., dietary and physical activity patterns). The longitudinal designs across the diverse populations should be employed by the Future studies through incorporating MRI and CT for visceral fat measurement and confirm the sex hormone influences directly assays. While the more comprehensive biomarkers (IL-6, TNF-α, HbA1c, HOMA-IR) were included as part of the study, the focus on direct measurements of testosterone and estradiol, properly standardized for menstrual phase, adds strength to the hormonal relationship yet still needs to be validated in larger cohorts. Interventions aimed at decreasing Fetuin-A and Nesfatin-1 through lifestyle changes (e.g., exercise or omega-3 diet) or treatments based on hormones may provide a novel treatment strategy and may also continue to elucidate mechanisms in a gender-specific manner.

Conflict of Interest: None declared.

Financial Disclosure: Self-funded; no external financial support received.

References

1. Annani-Akollor ME, Laing EF, Osei H, Mensah E, Owiredu EW, et al. (2019). Prevalence of metabolic syndrome and the comparison of fasting plasma glucose and HbA1c as the glycemic criterion for MetS definition in the non-diabetic population in Ghana. Diabetol Metab Syndr. 11:26.
2. Moraes MLD, Urrego IDC, Romero GR (2025). Waist circumference cut-off points for the definition of metabolic syndrome in older adults: SABE Colombia study. Cien Saude Colet. 30:e06692023.
3. Khadir A, Kavalakatt S, Madhu D, Hammad M, Devarajan S, et al. (2018). Fetuin-A levels are increased in the adipose tissue of diabetic obese humans but not in circulation. Lipids Health Dis. 17:291.
4. Birukov A, Polemiti E, Jäger S, Stefan N, Schulze MB (2022). Fetuin-A and risk of diabetes-related vascular complications: A prospective study. Cardiovasc Diabetol. 21:6.
5. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, et al. (2014). Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 384:766–781.
6. Blaska M, Gołąb-Jenerał K, Ziora K (2025). "Satiety molecules"—nesfatin-1 and glucagon-like peptide 1 in blood serum in patients with anorexia nervosa and obesity. Endokrynol Pol. 76:134–144.
7. Gharanei S, Ramanjaneya M, Patel AH, Patel V, Shabir K, et al. (2022). NUCB2/Nesfatin-1 reduces obesogenic diet-induced inflammation in mice subcutaneous white adipose tissue. Nutrients. 14:1409.
8. Wang Y, Koh WP, Jensen MK, Yuan JM, Pan A (2019). Plasma fetuin-A levels and risk of type 2 diabetes mellitus in a Chinese population: A nested case-control study. Diabetes Metab J. 43:474.

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667

9. Friedrich T, Stengel A (2021). Role of the novel peptide phoenixin in stress response and possible interactions with nesfatin-1. Int J Mol Sci. 22:9156.
10. Afrisham R, Hashemnia SM, Majidi Z, Mozaffari S, Vahidi M (2020). Association of fetuin-A with the pathogenesis of metabolic diseases. Int J Biomed Public Health. 3:95–102.
11. Öner-İyidoğan Y, Koçak H (2025). Interaction of fetuin-A with obesity related insulin resistance and diabetes mellitus. Turk J Biochem. 50:170–182.
12. Statistical Power Analysis for the Behavioral Sciences Cohen J (2013). Statistical Power Analysis for the Behavioral Sciences. Routledge.
13. Erkec OE, Milanlıoğlu A, Komuroglu AU, Kara M, Huyut Z, et al. (2021). Evaluation of serum ghrelin, nesfatin-1, irisin, and vasoactive intestinal peptide levels in temporal lobe epilepsy patients with and without drug resistance: A cross-sectional study. Rev Assoc Med Bras. 67:207–212.
14. Blüher M (2019). Obesity: Global epidemiology and pathogenesis. Nat Rev Endocrinol. 15:288–298.
15. Ma C, Cheng B, Zhou L, Cai S, Qin B, et al. (2024). Association between insulin resistance and vascular damage in an adult population in China: A cross-sectional study. Sci Rep. 14:18472.
16. Martin SS, Blaha MJ, Elshazly MB, Brinton EA, Toth PP, et al. (2013). Friedewald-estimated versus directly measured low-density lipoprotein cholesterol and treatment implications. J Am Coll Cardiol. 62:732–739.
17. Jansen HI, van Herwaarden AE, Huijgen HJ, Vervloet MG, Hillebrand JJ, et al. (2023). Lower accuracy of testosterone, cortisol, and free T4 measurements using automated immunoassays in people undergoing hemodialysis. Clin Chem Lab Med. 61:1436–1445.
18. Ramírez-Vélez R, Correa-Rodríguez M, Izquierdo M, Schmidt-RioValle J, González-Jiménez E (2018). Muscle fitness to visceral fat ratio, metabolic syndrome and ideal cardiovascular health metrics. Nutrients. 11:24.
19. Tchernof A, Després JP (2023). Obesity and Metabolic Syndrome. In Handbook of Obesity. pp. 503–510.
20. Rashid MA, Hoda MD, Ahmed F, Badiuzzaman M, Hossain A, et al. (2022). Short term outcome of obesity on cardiovascular responses in patient sample with SBP, DBP and heart rate. J Chittagong Med Coll Teach Assoc. 33:126–132.
21. Link JC, Reue K (2017). Genetic basis for sex differences in obesity and lipid metabolism. Annu Rev Nutr. 37:225–245.
22. Milyani AA, Al-Agha AE (2019). The effect of body mass index and gender on lipid profile in children and adolescents in Saudi Arabia. Ann Afr Med. 18:42–46.
23. Palmisano BT, Zhu L, Stafford JM (2017). Role of estrogens in the regulation of liver lipid metabolism. Sex Gender Factors Affect Metab Homeostasis Diabetes Obesity. 227–256.
24. Lee JW, Hong YM, Kim HS (2021). Identification of cardiovascular risk factors in obese adolescents with metabolic syndrome. Front Pediatr. 9:745805.
25. Rumińska M, Witkowska-Sędek E, Artemniak-Wojtowicz D, Krajewska M, Majcher A, et al. (2019). Changes in leukocyte profile and C-reactive protein concentration in overweight and obese adolescents after reduction of body weight. Cent Eur J Immunol. 44:307–315.
26. Arner P, Rydén M (2022). Human white adipose tissue: A highly dynamic metabolic organ. J Intern Med. 291:611–621.
27. Zhou ZW, Ju HX, Sun MZ, Chen HM, Fu QP, et al. (2018). Serum fetuin-A levels in obese and non-obese subjects with and without type 2 diabetes mellitus. Clin Chim Acta. 476:98–102.
28. Luo JJ, Wen FJ, Qiu D, Wang SZ (2021). Nesfatin-1 in lipid metabolism and lipid-related diseases. Clin Chim Acta. 522:23–30.
29. Peter A, Kovarova M, Staiger H, Machann J, Schick F, et al. (2018). The hepatokines fetuin-A and fetuin-B are upregulated in the state of hepatic steatosis and may differently impact on glucose homeostasis in humans. Am J Physiol Endocrinol Metab. 314:E266–E273.
30. Lu QB, Wang HP, Tang ZH, Cheng H, Du Q, et al. (2018). Nesfatin-1 functions as a switch for phenotype transformation and proliferation of VSMCs in hypertensive vascular remodeling. Biochim Biophys Acta Mol Basis Dis. 1864:2154–2168.
31. Lopez-Aguilar I, Ibarra-Reynoso LD, Malacara JM (2018). Association of nesfatin-1, acylated ghrelin and cortisol with scores of compulsion, food addiction, and binge eating in adults with normal weight and with obesity. Ann Nutr Metab. 73:54–61.
32. Pan X, Wen SW, Bestman PL, Kaminga AC, Acheampong K, et al. (2020). Fetuin-A in metabolic syndrome: A systematic review and meta-analysis. PLoS One. 15:e0229776.
33. Mo Q, Deng X, Zhou Z, Yin L (2025). High-fat diet and metabolic diseases: A comparative analysis of sex-dependent responses and mechanisms. Int J Mol Sci. 26:4777.
34. Ndzie Noah ML, Adzika GK, Mprah R, Adekunle AO, Adu-Amankwaah J, et al. (2021). Sex–gender disparities in cardiovascular diseases: The effects of estrogen on eNOS, lipid profile, and NFATs during catecholamine stress. Front Cardiovasc Med. 8:639946.
35. Iob E, Steptoe A (2019). Cardiovascular disease and hair cortisol: A novel biomarker of chronic stress. Curr Cardiol Rep. 21:116.
36. Draper CF, Duisters K, Weger B, Chakrabarti A, Harms AC, et al. (2018). Menstrual cycle rhythmicity: Metabolic patterns in healthy women. Sci Rep. 8:14568.
37. Wallace M, Hashim YY, Wingfield M, Culliton M, McAuliffe F, et al. (2010). Effects of menstrual cycle phase on metabolomic profiles in premenopausal women. Hum Reprod. 25:949–956.
38. Bourebaba L, Marycz K (2019). Pathophysiological implication of fetuin-A glycoprotein in the development of metabolic disorders: A concise review. J Clin Med. 8:2033.
39. Mauvais-Jarvis F (2017). Epidemiology of gender differences in diabetes and obesity. Sex Gender Factors Affect Metab Homeostasis Diabetes Obesity. 3–8.
40. Welch AA, Hayhoe RP, Cameron D (2020). The relationships between sarcopenic skeletal muscle loss during ageing and macronutrient metabolism, obesity and onset of diabetes. Proc Nutr Soc. 79:158–169.
41. Morán-Costoya A, Proenza AM, Gianotti M, Lladó I, Valle A (2021). Sex differences in nonalcoholic fatty liver disease: Estrogen influence on the liver–adipose tissue crosstalk. Antioxid Redox Signal. 35:753–774.

Citation: Kame NK (2026). The Physiological Effects of Fetuin-A and Nesfatin-1 on Metabolic Parameters in Obese and Non-Obese subjects. Int J Health Sci Biomed. 3(3): 1-10. DOI: 10.5281/zenodo.20973667