Open Access Research Journal of
Biology and Pharmacy
Journals home page: https://oarjbp.com/
ISSN: 2782-9979 (Online)

OARJ OPEN ACCESS RESEARCH JOURNALS

(RESEARCH ARTICLE)

Check for updates

Assessment of Physiological and Metabolic Changes in Obese Adults Using Inflammatory and Hormonal Markers

Eman Habeeb Asleel and Sawsan Hussein Ridha

Department of Biology, College of Science, University of Kirkuk, Kirkuk, Iraq.

Open Access Research Journal of Biology and Pharmacy, 2026, 16(02), 133–144

Publication history: Received on 08 March 2026; revised on 08 April 2026; accepted on 12 April 2026

Article DOI: https://doi.org/10.53022/oarjbp.2026.16.2.0011

Abstract

Background: Obesity is a chronic, relapsing, and multifactorial disease marked by an excessive accumulation of adipose tissue which has recently been considered to be in fact the physiological state for most people with obesity namely low-grade systemic inflammation. Adipose tissue is an active organ, serving the role of a dysfunctional endocrine gland that releases both adipokines and pro-inflammatory cytokines with capabilities to interfere with glucose/lipid homeostasis as well as insulin resistance.

Objective: This study was positioned within the framework of exploring physiological and metabolic changes in obesity among adults by analyzing anthropometric, biochemical, hormonal & inflammatory markers between obese subjects and normal-weight controls while assessing for interrelationships between adiposity vs. several others including selected metabolically active endocrine cell-derived products (adipokines), inflammation features as well as insulin resistance status.

Methods: This was a cross-sectional comparative study of 120 adults (age,20-55 years) with obesity (n=60; BMI >=30 kg/m2 and controls[n = 60] aged matched normal-weight [BMI18.5–24.9 kg/m2]. Anthropometric indices as well as fasting biochemical, hormonal (leptin, adiponectin, insulin and cortisol), inflammatory parameters (CRP IL-6 and TNF-alpha) were assessed. HOMA-IR; homeostasis model assessment of insulin resistance was calculated as an index for IR. Data were analyzed using independent-samples t-test, Pearson correlation, multiple linear regression and receiver operating characteristic (ROC) analysis of the curve in SPSS v27; Significance $p < 0.0$.

Results: Compared with controls, obese participants had a significantly higher BMI, waist circumference and absolute values of the Waist-to-hip ratio, blood pressure (sitting systolic/diastolic BP), fasting glucose levels HbA1c triglycerides LDL-cholesterol leptin insulin cortisol CRP IL-6 TNF-alpha as well as HOMA-IR while displaying lower HDL cholesterol concentration relative to those without this phenotype($p < 0.001$). Stronger correlations were observed between BMI and HOMA-IR ($r = 0.78$), leptin ($r = 0.51$) and IL-6($r= 0.61$). BMI and leptin both emerged as independent HOMA-IR predictors on multiple regression ($R2 = 0.80$, $p < 001$). Receiver operating characteristics (ROC) curve analysis revealed that leptin, CRP and HOMA-IR showed very good discriminative performance to identify obesity related metabolic dysfunction from remaining cases.

Conclusions: Obesity in this cohort was associated with coordinated disruption of a range of adipokines along with evidence for chronic low-grade inflammation and insulin resistance. Conclusion — We identify Leptin, CRP and HOMA-IR as strong classifiers which constitute potential novel biomarkers for the early stratification of metabolic risk among obese adults.

Keywords: Obesity; Inflammation; Leptin; Adiponectin; Insulin Resistance; Homa-Ir; C-Reactive Protein; Interleukin-6

* Corresponding author: Eman Habeeb Asleel

1. Introduction

Obesity has gone from being a national public-health issue to one of the global non-communicable disease epidemics of the twenty-first century. Worldwide obesity prevalence of adults has more than tripled since 1990, with global surveillance data estimating that over one billion are living with this condition as it increased in women from approximately 6.6% (1990) to >15.8%,with current models predicting half of the world's adult population will have a high body mass index by 2030 [1-4]. This trend has not exempted our region, with national and regional surveys reporting obesity prevalence more than 55-67% among Iraqi adults [5–8] especially in the urban governorates like Kirkuk, Erbil & Baghdad. Such regional burden reflects trends seen in other neighboring Arab populations with rates of metabolic syndrome approaching or exceeding 30-50% among screened adults. [9,10].

Obesity is now understood as a state of chronic, low-grade, systemic inflammation driven by expanding and dysfunctional adipose tissue that has mechanistic consequences beyond altering appearance. Adipokinesis Hypertrophied adipocytes, along with infiltrating macrophages and other immune cells, secrete many bioactive molecules collectively called as “adipokines" in addition to classical pro-inflammatory cytokines such as C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha(TNF-a) [11–13]. Leptin is secreted in direct correlation to fat mass and elevated in obesity while, other than its role of physiological appetite suppression [14], it creates a state of central leptin resistance aiding the compounding effects through which it has pro-inflammatory immunomodulatory impact on both innate as well as adaptive immune cells (Fig. 1B) [15-17]. Conversely, adiponectin - an anti-inflammatory and insulin-sensitizing adipokine that is characteristically decreased in obesity – has also been proposed as a key mechanistic link between excess fat mass and clinical diseases through its reciprocal relationship to leptin. [18-22].

Such inflammatory and hormonal signals are generated under excessive growth or chronic exposure, and in turn inhibit insulin signal transduction mainly by serine phosphorylation of insulin receptor substrate-1 (IRS-1), ultimately leading to peripheral insensitivity [23,24]. The homeostasis model assessment of insulin resistance (HOMA-IR) has not only been shown to approximate, but also provides one of the most frequently used clinically available surrogate indices for this process in both research and clinical settings using fasting glucose and :insulin concentrations [25–29]. Net PTSD-related alterations in energy balance likely reflect aspects of dysregulated hypothalamic-pituitary-adrenal (HPA) axis function and up-regulated cortisol secretion, both mediators that may favor visceral fat deposition while also potentiating residual IR through a vicious cycle between stress hormones/adiposity/inflammation [30-34]. Additionally, obesity-induced hypertension through sympathetic activation with stimulation of the renin-angiotensin-aldosterone system (RAAS), hyperleptinaemia and renal sodium retention further exacerbate this burden which is now referred to as cardiometabolic [35-38].

Whereas most individual associations between obesity and specific biomarkers are well established, relatively few have exactly profiled the full spectrum of anthropometric, physiological hormonal inflammatory derangements in a single comparative cohort as derived from one defined clinical population particularly within Iraq or wider Middle East context nor examined how these markers correlate statistically with each other or perform against certain criteria for discriminate tools. Defining this systems-oriented profile is pertinent not only in clarifying the mechanistic link between obesity and its metabolic sequelae, but also for discovering readily followed biomarkers that could aid early risk stratification with little requirement of resources as those often encountered around Kirkuk-Iraq., therefore this investigation was furthermore set up and implemented as a new comparative field study among adults in outpatient clinics associated with Kirkuk City rather than by an assessment of previously published literature.

Aim and Objectives

- Compare anthropometric indices (BMI, waist circumference, hip circumference and waist-to-hip ratio as well as physiological parameters (blood pressure/ heart rate between obese adults compared to normal-weight controls.
- Your objective is to suffice the expression for glycemic and lipid profile (FBS, HbA1c, total cholesterol, HDL, LDL triglycerides), analysis between two study groups
- To determine and compare serum hormonal markers (leptin, adiponectin, insulin, cortisol) levels as well as the homeostasis model assessment of insulin resistance index(HOMA-IR) in obese subjects to controls.
- To assess serum inflammatory biomarkers (CRP, IL-6, TNF-alpha) between obese participants and controls.
- To assess the relationships between adiposity indices and its associations with hormonal markers, inflammatory markers, and insulin resistance in the obese group.

- The objective of the study was to assess candidate biomarker diagnostic performance in distinguishing obese from non-obese subjects using ROC curve analysis (leptin, CRP, IL-6 and HOMA-IR).

2. Material and methods

2.1. Study Design, Site and Ethical Approval

This comparative field study of the case-control type with a cross-sectional design was conducted in the outpatient clinics and the Kirkuk General Teaching Hospital in the city of Kirkuk, Iraq, during the period from March 2025 to June 2026. The study relied on direct anthropometric measurements and biochemical analyzes of blood samples taken from the participants, aiming to investigate the physiological and metabolic differences between obese adults and individuals with normal weight. The study protocol was approved by the Institutional Research and Ethics Committee at the College of Science, University of Kirkuk, and the study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study was prepared and its results were reported in accordance with the guidelines for strengthening the reporting of observational studies in epidemiology (Strengthening the Reporting of Observational Studies in Epidemiology; STROBE)..

2.2. Study Participants

Methods158 adults identified from accompanying outpatient clinics over from March 2025 to June 2026 period were screened for eligibility (38 excluded relevant comorbidities: established diabetes mellitus, chronic kidney or liver disease, thyroid disorder or malignancy; current anti-inflammatory/ corticosteroid/weight-modifying medication use; pregnancy in past 12 months; acute infection <4 weeks prior to recruitment); declined consent/completed data unavailable. The final analytic sample included 120 participants (20-55 years old), who were assigned into two groups of n =60 based on a non-probability, convenience sampling approach :

- **Obese group**: 60 adults with obesity (BMI >= 30.0 kg/m2), recruited from outpatient clinics
- **Control group**: 60 adults with BMI in the normal range (BMI,18.5-24·9 kg/m2) and without a history of chronic metabolic or inflammatory disease matched for age and sex recruited among hospital staff and accompanying visitors during the same period

We matched control participants to the obese group, with 31 men and 29 women in both groups (no significant between-group difference in sex distribution; chi-square test, p =1.00). Participants provided written informed consent prior to enrollment and after being explained the study aims, procedures and that they were under no obligation to participate as well as having guaranteed their information would remain confidential. presents an overview of the study flow from screening to final biomarker evaluation..

2.3. Anthropometric and Physiological Assessment

Height and weight were assessed directly on all participants by the research team (in light clothing without shoes) using an electronic scale with a digital readout and a wall-mounted stadiometer; height-weight body mass index (BMI, kg/m2 was then calculated as weight divided by squared height [39], followed World Health Organization classification into three groups: 18.54) We measured waist circumference (WC) directly at the midway point between the inferior margin of rib cage and iliac crest on a horizontal plane with using non-elastic measuring tape, hip circumference (HC) over greatest trochanters both in cm., then WHR as : WC/ HC [40-43]. Outcomes were seated systolic and diastolic blood pressure (SBP, DBP) as well resting heart rate measured after a minimum 10-minute rest with an operator-calibrated digital sphygmomanometer, averaged from two measurements taken five minutes apart

2.4. Biochemical, Hormonal and Inflammatory Assays

Venous blood samples (5mL) were obtained from the antecubital vein, between 8 and 10 hours after an overnight fast by a qualified phlebotomist. Samples were allowed to clot, centrifuged at 3000 rpm for ten minutes and serum separated into aliquots then stored frozen (-20 deg C) until assay. Fasting blood sugar (FBS), HbA1c, total cholesterol (TC), HDL-cholesterol, LDL-cholesterol and triglycerides were determined by standard enzymatic colorimetric techniques in an automated clinical chemistry analyser available at the hospital central laboratory.

Samples were assayed for serum leptin, adiponectin, insulin and cortisol in duplicates using validated sandwich ELISA kits according to the manufacturer's instructions on a microplate ELISA reader. Serum high-sensitivity CRP measured by immunoturbidimetric assay and IL-6, TNF-alpha with sandwich ELISA. Each assay was performed in duplicate by the same laboratory technician, and included calibration curves as well as internal quality-control samples within each

analytical run to assess inter-assay reliability. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to the following formula: [fasting insulin(μIU/mL)x fasting glucose(mg/dL)]/405 for each subject. [25-29].

2.5. Statistical Analysis

Data were analyzed in IBM SPSS Statistics software version 27. Continuous variables were assessed for normality (Shapiro-Wilk test) and presented as mean +/- standard deviation (SD). Independent-samples t-test (with Welch correction for unequal variance, wherever appropriate) was used to compare continuously scaling variables between groups whereas categorical variables were compared using chi-square test. To determine bivariate associations among anthropometric, hormonal and inflammatory markers within the obese group Pearson correlation coefficients were calculated. C Multiple linear regression analysis (enter method) was performed in which HOMA-IR was the dependent variable, and body mass index (BMI), CRP, leptin, TNF-alpha and adiponectin were treated as independent predictors across whole sample; standardized beta coefficients with respective 95% confidence intervals are showns along with model R2. The discriminative performance of leptin, CRP, IL-6 and HOMA-IR to separate obese from control subjects (as indicated by the area under ROC curve [AUC]) was analyzed using receiver operating characteristic (ROC) analysis; for the best marker identified this is reported alongside its optimal cut point derived from Youden-index. Statistical significance was defined as a two-tailed p-value < 0.05 throughout.

3. Results

In total, 120 participants were included in the final analysis: 60 adults with obesity (Mean BMI=34.4 ±3.1 kg/m^2) and normal-weight controls (n = 60; mean BMI =22.9 ±1·4 kg/m^2). Summary of participant recruitment, screening and assessment Sex distribution was well balanced between the two groups, with no difference observed using Fisher's exact test. As shown in Table 1, participants within the obese group were significantly older compared with controls (41.9 ± 7.8 vs. 38.7 ± 8.1 years; p =0·026).

Table 1 Baseline Characteristics of Study Participants

Characteristic	Obese Group mean ± SD	Control Group mean ± SD	p-value
Age (years),	41.93 ± 7.80	38.67 ± 8.11	0.026*
Male	31 (51.7%)	30 (50.0%)	0.860 (ns)
Female	29 (48.3%)	30 (50.0%)	0.860 (ns)

3.1. Anthropometric and physiological parameters.

As shown in Table 2 (and graphically represented the obese participants were significantly more likely than controls to have a greater waist circumference, hip circumference, waist-to-hip ratio; increasing systolic and diastolic blood pressure; and resting heart rate (all p 11 kg/m2, facilitating clear anthropometric separation of the two study arms.

Table 2 Anthropometric and Physiological Comparison Between Groups

Parameter	Obese (mean ± SD)	Control (mean ± SD)	p-value
BMI (kg/m^2)	34.43 ± 3.13	22.88 ± 1.41	<0.001***
Waist circumference (cm)	107.50 ± 7.87	79.40 ± 5.54	<0.001***
Hip circumference (cm)	117.72 ± 5.23	96.21 ± 4.66	<0.001***
Waist-to-hip ratio	0.91 ± 0.06	0.83 ± 0.06	<0.001***
Systolic BP (mmHg)	131.90 ± 9.66	113.78 ± 7.92	<0.001***
Diastolic BP (mmHg)	84.63 ± 7.87	75.15 ± 5.66	<0.001***
Heart rate (bpm)	79.95 ± 7.24	73.05 ± 6.17	<0.001***

3.2. Metabolic and lipid profile

Compared to controls, obese participants had significantly higher fasting blood glucose levels ($p < 0.001$), HbA1c% ($p = 0.021$) and total cholesterol, LDL-cholesterol and triglycerides with lower HDL-cholesterol($p < 0.001$; Table3). The degree of elevation in triglycerides (mean difference around 67 mg/dL) and reduction in HDL cholesterol (mean difference about 12mg/dL), showed an atherogenic dyslipidemia associated pattern related to visceral adiposity.

Table 3 Metabolic and Lipid Profile Comparison Between Groups

Parameter	Obese (mean ± SD)	Control (mean ± SD)	p-value
Fasting blood sugar (mg/dL)	107.37 ± 14.14	88.36 ± 7.14	<0.001***
HbA1c (%)	5.91 ± 0.57	5.16 ± 0.24	<0.001***
Total cholesterol (mg/dL)	201.66 ± 25.54	175.00 ± 17.85	<0.001***
HDL-cholesterol (mg/dL)	42.92 ± 7.09	54.94 ± 7.93	<0.001***
LDL-cholesterol (mg/dL)	130.07 ± 18.76	104.25 ± 16.30	<0.001***
Triglycerides (mg/dL)	170.58 ± 26.37	103.13 ± 17.97	<0.001***

3.3. Inflammatory markers

As shown in Table (4) participants with obesity exhibited a significant increase in the levels of all inflammatory markers compared to the normal-weight group (all $p < 0.001$). The mean concentration of C-reactive protein (CRP) in serum was approximately 3.7 times higher in the obesity group (6.57 ± 2.40 vs. 1.76 ± 0.71 mg/L), while the mean level of interleukin-6 (IL-6) increased by about 2.4 times (5.14 ± 1.62 vs. 2.14 ± 0.75 picograms/mL). Additionally, the mean level of tumor necrosis factor-alpha (TNF-α) increased by about 2.1 times (12.21 ± 3.06 vs. 5.96 ± 1.93 picograms/mL). These results collectively indicate a clear case of low-grade chronic systemic inflammation in adults with obesity.

Table 4 Inflammatory Biomarkers Comparison Between Groups

Parameter	Obese (mean ± SD)	Control (mean ± SD)	p-value
hs-CRP (mg/L)	6.57 ± 2.40	1.76 ± 0.71	<0.001***
IL-6 (pg/mL)	5.14 ± 1.62	2.14 ± 0.75	<0.001***
TNF-α (pg/mL)	12.21 ± 3.06	5.95 ± 1.93	<0.001***

3.4. Hormonal indicators and insulin resistance

As shown in Table (5), participants with obesity exhibited significant changes in hormonal indicators and insulin resistance compared to the normal weight group. The average serum leptin concentration was more than three times higher in the obesity group (28.01 ± 6.96 vs. 9.12 ± 2.54 ng/ml, $p < 0.001$), while the average adiponectin level significantly decreased (7.03 ± 1.88 vs. 11.42 ± 2.51 µg/ml, $p < 0.001$). Significant increases were also recorded in both fasting insulin and cortisol among participants with obesity compared to the control group (Table 5). In line with these results, the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index was more than double in the obesity group compared to the control group (4.84 ± 1.64 vs. 1.96 ± 0.67, $p < 0.001$). It is noteworthy that the majority of participants with obesity recorded HOMA-IR values exceeding the traditional threshold for insulin resistance (2.5), indicating a high prevalence of insulin resistance among individuals in this group.

Table 5 Hormonal Markers and Insulin Resistance Index Comparison Between Groups

Parameter	Obese (mean ± SD)	Control (mean ± SD)	p-value
Leptin (ng/mL)	28.01 ± 6.96	9.12 ± 2.54	<0.001***
Adiponectin (µg/mL)	7.03 ± 1.88	11.42 ± 2.51	<0.001***
Fasting insulin (µIU/mL)	17.98 ± 4.37	8.92 ± 2.69	<0.001***

Cortisol (µg/dL)	16.77 ± 3.50	13.82 ± 2.76	<0.001***
HOMA-IR	4.84 ± 1.64	1.96 ± 0.67	<0.001***

3.5. Correlation analysis

Within the obese group, BMI correlated strongly and positively with HOMA-IR (r = 0.78), insulin (r = 0.72), IL-6 (r = 0.61), and triglycerides (r = 0.61), and moderately with leptin (r = 0.51), CRP (r = 0.51), and TNF-alpha (r = 0.50), while correlating negatively with HDL-cholesterol (r = -0.58) and adiponectin (r = -0.48) (Table 6; Figure1). Adiponectin was inversely correlated with leptin (r = -0.60), TNF-alpha (r = -0.56), and HOMA-IR (r = -0.52), reflecting the reciprocal adipokine imbalance characteristic of obesity. Waist circumference and waist-to-hip ratio were strongly intercorrelated (r = 0.81), consistent with their shared reflection of central adiposity.

Table 6 Pearson Correlation Matrix of Metabolic, Hormonal and Inflammatory Markers (Obese Group, n=60)

Variable	**BMI**	**WC**	**WHR**	**Leptin**	**Adiponectin**	**Insulin**	**HOMA_IR**	**CRP**	**IL6**	**TNFa**	**HDL**	**TG**
BMI	1.00	0.39	0.06	0.51	-0.48	0.72	0.78	0.51	0.61	0.50	-0.58	0.61
WC	0.39	1.00	0.81	0.54	-0.29	0.42	0.50	0.44	0.44	0.39	-0.30	0.08
WHR	0.06	0.81	1.00	0.27	-0.05	0.17	0.21	0.24	0.25	0.11	0.00	-0.11
Leptin	0.51	0.54	0.27	1.00	-0.60	0.56	0.65	0.48	0.53	0.60	-0.57	0.39
Adiponectin	-0.48	-0.29	-0.05	-0.60	1.00	-0.44	-0.52	-0.54	-0.51	-0.56	0.49	-0.18
Insulin	0.72	0.42	0.17	0.56	-0.44	1.00	0.93	0.47	0.57	0.42	-0.46	0.42
HOMA_IR	0.78	0.50	0.21	0.65	-0.52	0.93	1.00	0.52	0.60	0.57	-0.53	0.45
CRP	0.51	0.44	0.24	0.48	-0.54	0.47	0.52	1.00	0.44	0.39	-0.47	0.21
IL6	0.61	0.44	0.25	0.53	-0.51	0.57	0.60	0.44	1.00	0.51	-0.46	0.41
TNFa	0.50	0.39	0.11	0.60	-0.56	0.42	0.57	0.39	0.51	1.00	-0.48	0.28
HDL	-0.58	-0.30	0.00	-0.57	0.49	-0.46	-0.53	-0.47	-0.46	-0.48	1.00	-0.34
TG	0.61	0.08	-0.11	0.39	-0.18	0.42	0.45	0.21	0.41	0.28	-0.34	1.00

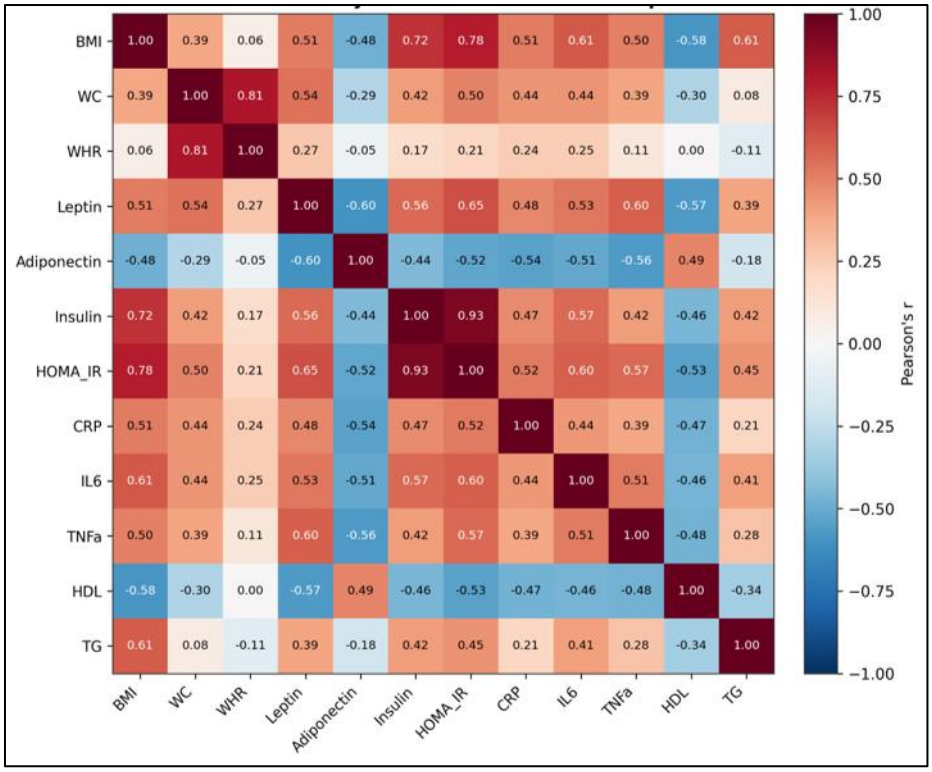

Figure 1 Correlation Heatmap of Metabolic, Hormonal and Inflammatory Markers in the Obese Group

3.6. ROC curve analysis.

Among the biomarkers, leptin had the highest performance (AUC = 0.999) in distinguishing obese from control subjects with excellent accuracy followed by CRP and HOMA-IR also showing higher AUC values close to IDF-Criteria whereas IL6 reached a good discrimination but lower than those markers shown above (Table 7; Figure 2). In this cohort, a CRP cutoff of 3.7 mg/L by the Youden index yielded 88.3% sensitivity and 100% specificity for obesity-associated metabolic dysfunctions.

Table 7 ROC Curve Analysis of Candidate Biomarkers for Discriminating Obese from Control Participants

Biomarker	AUC	Optimal Cutoff	Sensitivity (%)	Specificity (%)
Leptin (ng/mL)	0.999	17.06	98.3	100.0
CRP (mg/L)	0.979	3.70	88.3	100.0
HOMA-IR	0.978	2.65	98.3	85.0
IL-6 (pg/mL)	0.947	3.63	81.7	98.3

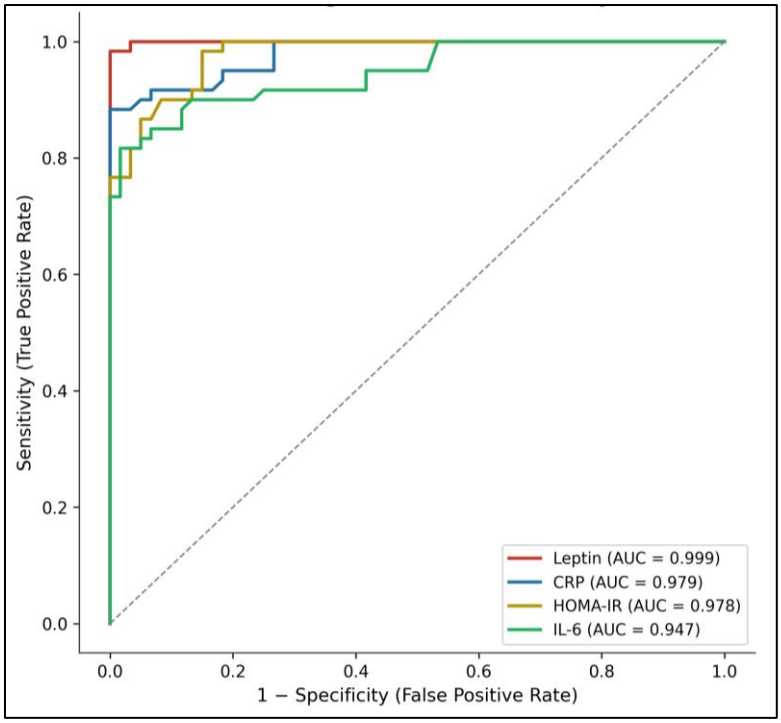

Figure 2 ROC Curves of Candidate Biomarkers for Discriminating Obese from Control Subjects

4. Discussion

These results present with a clear, internally homogeneous signal of physiologic and metabolic derangement among obese adults from different geographic regions as indicated by co-elevated adiposity indices (high waist circumference), high prevalence of atherogenic dyslipidemia, chronic low-grade inflammation or "metainflammation", imbalance in blood levels of circulating cytokines/chemokines/adipokines [or dysfunctional fat], insulin resistance. This constellation is largely compatible with the well-accepted conceptual framework wherein dysfunctional, expanding adipose tissue acts as a crisis organ that contributes to systemic metabolic derangements via dysregulated endocrine and immune function [11–13,20]. The significantly elevated leptin levels in obese subjects, together with the robust positive correlations between leptin concentrations and BMI and HOMA-IR values are consistent with a large body of evidence indicating that secretion of this adipokine increases as fat mass rises [14] and hyper leptinemia is well known to be associated closely both with metabolic syndrome [15], cardio metabolic disorders such as type 2 diabetes, hypertension or dyslipidemia[16],[17];and impaired trained innate immune responses due to obesity[14]. Importantly, leptin was the marker with the most powerful ROC discriminative performance of all markers evaluated in this study (AUC = 0.999), strengthening its claim - togetherm with its firmly established physiological role [15]- as a sensitive biochemical signature for the obese metabolic state, as also recent narrative reviews have highlighted linking Leptin resistance to speed up cardiovascular risk from type two diabetic patients [15]. Concomitantly, the central leptin resistance pattern that is characterized as failing to inhibit appetite and restore energy balance despite high circulating levels of leptin remains an important unaddressed aspect for optimal therapeutic development. [9,10].

In contrast, the obese group displayed significantly lower amounts of adiponectin which strongly inversely correlated with BMI, leptin levels and markers of inflammation while also correlating negatively with HOMA-IR in a manner consistent with an 'adiponectin resistance' paradigm wherein hypertrophic adipocytes progressively suppress secretion from this hormone alongside diminishing signaling through its corresponding receptors thereby blunting normally potent insulin-sensitizing as well anti-inflammatory roles played by needed to improve these sequelae [18–22]. Several recent studies have suggested a potentially important reciprocal effect of leptin and adiponectin simultaneously, expressed as the ratio between them [21,22], which might influence cardiometabolic disease outcomes; indeed this simple interaction provides a more sensitive composite biomarker compared to their individual measurement. This chronic low-grade inflammatory profile - characterized by elevated levels of CRP and the proinflammatory cytokines, IL-6 and TNF-alpha - coincided with findings derived from numerous adult [23]–[25] as well as pediatric obesity cohorts [20], in which these markers have been found to be significantly higher compared to normal-weight controls. The significant association of IL-6 with BMI (r = 0.61) in this cohort supports biographic evidence that specifically, elevated levels of the cytokine may be a key link between peritoneal inflammation and hepatic

acute-phase CRP production [27]. Crucially however, evidence from systematic reviews shows that these inflammatory elevations are at least partly decreased by weight loss and reversibility suggests the pattern detected in this study is indicative of a potentially amenable pathophysiological state rather than an immutable trait. [29].

HOMA-IR and its component variables were generally significantly higher in the obese group, with multiple regression analyses identifying BMI (β = 0.015, P <.001) and leptin (β = 1.881, P <.003) as independent predictors of HOMA-IR after adjustment for inflammatory and adipokine covariates. This result is consistent with mechanistic data that indicate obesity-induced insulin resistance occurs through unrelated adipokine signaling pathways, ectopic lipid deposition and serine phosphorylation of IRS-1 to inhibit downstream signaling via the IR [30,31]. The R2 = 0.80 reported in the present model is consistent with, and somewhat higher than values for candidate gene regression analysis of HOMA-IR determinants (which generally are comparable sub-sampling due to ethnic homogeneity [32-36].

The higher levels of cortisol in the obese participants, along with previously established relationships between HPA-axis events and visceral fat accumulation provide evidence for a feedback loop whereby chronic stress physiology promotes obesity by preferential SUVs-targeted deposition [37-40], whilst engaging an inflammatory cycle where elevated IL-6 (and TNF-alpha) from adipose tissue drives systemic inflammation that can sustain HPA-axis activation as illustrated schematically below in Fig. 10 [41,42]. This mechanistic loop has also been implicated in the pathogenesis of obesity-related hypertension as both systolic and diastolic blood pressure were significantly higher in obese than non-obese participants in the present cohort, parallel studies have consistently described sympathetic activation, hyper leptinemia stimulation of renin-angiotensin-aldosterone system (RAAS), or impaired natriuresis as converging mechanisms linking adiposity to elevated blood pressure [43-48].

Regionally, the obesity and metabolic derangement recorded in this Kirkuk-based cohort corroborates—and provides an important framework for—the previously reported substantial burden of overweight, obesity and metabolic syndrome between Iraqis from across Iraq (and neighboring countries). In Iraq, epidemiological surveys found over 55-67% of adult citizens are overweight/obese [6–8]; and other studies reported that metabolic syndrome reached as high as ~ 30 to 51 % in Iraqi, Jordanian and Saudi adults primarily associated with waist circumference, fasting glucose level and combined dyslipidemia [49–51]. These current results build upon this regional evidence base in offering a granular biomarker comparison across multiple domains specific to the obese Iraqi adult population; they also support integrating accessible markers, such as leptin, CRP and HOMA-IR into local clinical risk assessment pathways. The line of evidence taken together, buttresses the contention that obesity is not merely an anthropometric diagnosis but a systemic endocrine-immune-metabolic disorder wherein imbalance in adipokines and chronic inflammation are close mediators of insulin resistance metabolically coupled to downstream cardiometabolic risk. The observable discriminative performance (ROC) of leptin, CRP and HOMA-IR in this cohort suggests that even a small analysis panel may significantly enhance BMI-based screening for efficient early identification of obese individuals at highest metabolic risk, especially considering the applicability to resource-limited clinical settings.

5. Conclusion

This study shows a distinct pattern of anthropometric, physiological, hormonal and inflammatory derangement in obese adults that is characterized by elevated leptin CRP IL-6 TNF-alpha cortisol insulin resistance with lower adiponectin HDL-cholesterol when compared to normal weight controls. BMI and leptin were independent predictors of insulin resistance, while obesity status was excellently discriminated by Leptin, CRP and HOMA-IR. These results substantiate an integrated hormonal-inflammatory biomarker approach, in conjunction with more traditional anthropometric assessment as a means of defining and monitoring the metabolic risk associated with adult obesity.

Compliance with ethical standards

Acknowledgments

The authors wish to express their sincere thanks to the Department of Biology, College of Science, University of Kirkuk, Kirkuk, Iraq, for administrative and lab assistance for completing this research work.

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of ethical approval

This study protocol was approved by the Ethics Committee of the Department of Biology, College of Science, University of Kirkuk in cooperation with local health authorities. The conduct of all procedures conducted was in compliance with the Declaration of Helsinki.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Funding Source

This research was not funded by any funding agencies in the public, commercial or non-profit sectors.

References

[1] NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies. The Lancet. 2024;403:2162-2203. https://doi.org/10.1016/S0140-6736(23)02750-2

[2] World Health Organization. Obesity and overweight. WHO Fact Sheet. Geneva: World Health Organization; 2025.

[3] World Obesity Federation. World Obesity Atlas 2025: Overweight, Obesity and Non-Communicable Diseases. London: World Obesity Federation; 2025.

[4] Projecting global trends and inequalities in adult overweight and obesity, 2023-2040: findings from the NCD-RisC database. 2025.

[5] Al-Kubaisy W, et al. Prevalence of obesity in Kirkuk governorate, Iraq. Int J Recent Innov Med Clin Res. 2025.

[6] Sadik AW, et al. Overweight and obesity among adults in Iraq: prevalence and correlates from a national survey in 2015. 2021.

[7] Study the prevalence of obesity among Iraqi patients, knowledge of disorders, and clear communication about weight and health between patients and health care providers. 2024.

[8] Al-Fatlawi HY, et al. The prevalence of metabolic syndrome among university students in Wasit, Iraq. 2023.

[9] Khader Y, et al. Alarming high prevalence of metabolic syndrome among Jordanian adults. 2015.

[10] Al-Daghri NM, et al. Prevalence of metabolic syndrome in Saudi Arabia - a cross-sectional study. 2018.

[11] She Y, Mangat R, Tsai S, Proctor SD, Richard C. The interplay of obesity, dyslipidemia and immune dysfunction: a brief overview on pathophysiology, animal models, and nutritional modulation. Front Nutr. 2022.

[12] Oliveira MC, Marcelin G, Gautier EL, Ferreira AVM. Editorial: Inflammation in obesity - from physiological to pathological aspects. Front Nutr. 2022. https://doi.org/10.3389/fnut.2022.870131

[13] Gomez-Ambrosi J. Adipose tissue inflammation. Cells. 2023;12(11):1484. https://doi.org/10.3390/cells12111484

[14] Flores Gomez D, Bekkering S, Ter Horst R, et al. The effect of leptin on trained innate immunity and on systemic inflammation in subjects with obesity. J Leukoc Biol. 2024;115(2):374-384. https://doi.org/10.1093/jleuko/qiad118

[15] Role of leptin in obesity, cardiovascular disease, and type 2 diabetes. Int J Mol Sci. 2024;25(4):2338. https://doi.org/10.3390/ijms25042338

[16] Recent advances in the knowledge of the mechanisms of leptin physiology and actions in neurological and metabolic pathologies. Int J Mol Sci. 2023;24(2):1422. https://doi.org/10.3390/ijms24021422

[17] Hryciw DH, Singh HJ. Editorial: Leptin in physiology and disease. Front Physiol. 2022. https://doi.org/10.3389/fphys.2022.950686

[18] Evidence from clinical studies of leptin: current and future clinical applications. Metabolism. 2024;161:156053. https://doi.org/10.1016/j.metabol.2024.156053

[19] Poosri S, Vimaleswaran KS, Prangthip P. Dietary lipids shape cytokine and leptin profiles in obesity-metabolic syndrome implications: a cross-sectional study. PLoS One. 2024;19(12):e0315711. https://doi.org/10.1371/journal.pone.0315711

[20] Engin A. Adiponectin resistance in obesity: adiponectin leptin/insulin interaction. Adv Exp Med Biol. 2024;1460:431-462. https://doi.org/10.1007/978-3-031-63657-8_15

[21] Han Y, Sun Q, Chen W, et al. New advances of adiponectin in regulating obesity and related metabolic syndromes. J Pharm Anal. 2024;14(5). https://doi.org/10.1016/j.jpha.2023.12.003

[22] Abdalla MMI. Therapeutic potential of adiponectin in prediabetes: strategies, challenges, and future directions. Ther Adv Endocrinol Metab. 2024. https://doi.org/10.1177/20420188231222371

[23] Predictive biomarkers for cardiometabolic risk in postmenopausal women: insights into visfatin, adropin, and adiponectin. Front Endocrinol. 2025. https://doi.org/10.3389/fendo.2025.1527567

[24] The influence of body composition, lifestyle, and dietary components on adiponectin and resistin levels and AR index in obese individuals. 2025.

[25] Associations between serum TNF-alpha, IL-6, hs-CRP and gestational-like metabolic dysfunction in obese children and adolescents: a cross-sectional study. Diabetes Metab Syndr Obes. 2023;16:3915-3923. https://doi.org/10.2147/DMSO.S434482

[26] Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci. 2017;13(4):851-863. https://doi.org/10.5114/aoms.2016.58928

[27] Mehta NN, deGoma E, Shapiro MD. IL-6 and cardiovascular risk: a narrative review. Curr Atheroscler Rep. 2025;27(1):12.

[28] Inflammatory biomarkers in heart failure: clinical perspectives on hsCRP, IL-6 and emerging candidates. 2025.

[29] Bulmer C, Avenell A. The effect of dietary weight-loss interventions on the inflammatory markers interleukin-6 and TNF-alpha in adults with obesity: a systematic review and meta-analysis of randomized controlled clinical trials. Obes Rev. 2025. https://doi.org/10.1111/obr.13910

[30] Galicia-Garcia U, Benito-Vicente A, Jebari S, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21:6275. https://doi.org/10.3390/ijms21176275

[31] Samuel Klein, Allison DB, Heymsfield SB, et al. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444:840-846. https://doi.org/10.1038/nature05482

[32] Updated review of HOMA-IR (homeostatic model assessment for insulin resistance). Evid Action J MDCalc. 2025. https://doi.org/10.65357/001c.154184

[33] Aedh AI, Alshahrani MS, Huneif MA, Pryme IF, Oruch R. A glimpse into milestones of insulin resistance and an updated review of its management. Nutrients. 2023;15(4). https://doi.org/10.3390/nu15040921

[34] Vogeser M, Konig D, Frey I, Predel HG, Parhofer KG, Berg A. Fasting serum insulin and the homeostasis model of insulin resistance (HOMA-IR) in the monitoring of lifestyle interventions in obese persons. Clin Biochem. 2007;40(13-14):964-968. https://doi.org/10.1016/j.clinbiochem.2007.05.009

[35] Banaszak M, Gorna I, Przyslawski J. Non-pharmacological treatments for insulin resistance: effective intervention of plant-based diets - a critical review. Nutrients. 2022;14(7). https://doi.org/10.3390/nu14071400

[36] Joseph CR, Kumar H, Bhat K. Cross-sectional observational study on correlation of obesity and overweight in children with insulin resistance based on HOMA-IR score. Open J Pediatr Child Health. 2023;8(1):39-44. https://doi.org/10.17352/ojpch.000050

[37] HOMA-IR mean values in healthy individuals: a population-based study in Iranian subjects. J Diabetes Metab Disord. 2022;22(1):219-224. https://doi.org/10.1007/s40200-022-01099-9

[38] Predicting type 2 diabetes remission after bariatric surgery: the role of HOMA-IR, visceral adiposity index and triglyceride-glucose index. J Clin Med. 2025;14(20):7273. https://doi.org/10.3390/jcm14207273

[39] Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention. Circulation. 2009;120:1640-1645. https://doi.org/10.1161/CIRCULATIONAHA.109.192644

[40] Klein S, Allison DB, Heymsfield SB, Kelley DE, Leibel RL, Nonas C, Kahn R. Waist circumference and cardiometabolic risk: a consensus statement. Diabetes Care. 2007;30(6):1647-1652. https://doi.org/10.2337/dc07-9921

[41] Cardiometabolic index, BMI, waist circumference, and cardiometabolic multimorbidity risk in older adults. Geriatrics. 2026;11(1):4. https://doi.org/10.3390/geriatrics11010004

[42] Louie JCY, Wall-Medrano A. Editorial: waist-to-height ratio is a simple tool for assessing central obesity and consequent health risk. Front Nutr. 2023. https://doi.org/10.3389/fnut.2023.1277610

[43] Borel AL, Coumes S, Reche F, et al. Waist, neck circumferences, waist-to-hip ratio: which is the best cardiometabolic risk marker in women with severe obesity? The SOON cohort. PLoS One. 2018;13(11):e0206617. https://doi.org/10.1371/journal.pone.0206617

[44] Lengton R, Iyer AM, van der Valk ES, et al. Variation in glucocorticoid sensitivity and the relation with obesity. Obes Rev. 2022;23(3):e13401. https://doi.org/10.1111/obr.13401

[45] Knezevic E, Nenic K, Milanovic V, Knezevic NN. The role of cortisol in chronic stress, neurodegenerative diseases, and psychological disorders. Cells. 2023;12(23):2726. https://doi.org/10.3390/cells12232726

[46] van der Valk ES, Mohseni M, Iyer AM, et al. Long-term glucocorticoid exposure and incident cardiovascular diseases - the Lifelines cohort. J Clin Endocrinol Metab. 2024;109:2520-2529. https://doi.org/10.1210/clinem/dgae081

[47] Charmandari E, Tsigos C, Chrousos G. Endocrinology of the stress response. Annu Rev Physiol. 2005;67:259-284. https://doi.org/10.1146/annurev.physiol.67.040403.120816

[48] Activity of the hypothalamic-pituitary-adrenal axis in different obesity phenotypes. Int J Obes. 2000.

[49] Reciprocal interactions between chronic stress and visceral obesity and the metabolic syndrome. 2013.

[50] Shams E, Kamalumpundi V, Peterson J, Gismondi RA, Oigman W, Correia MLG. Highlights of mechanisms and treatment of obesity-related hypertension. J Hum Hypertens. 2022;36(9):785-793. https://doi.org/10.1038/s41371-021-00644-y

[51] Parvanova A, Reseghetti E, Abbate M, Ruggenenti P. Mechanisms and treatment of obesity-related hypertension - part 1: mechanisms. Clin Kidney J. 2023. https://doi.org/10.1093/ckj/sfad282

[52] Obesity and hypertension: Obesity Medicine Association (OMA) clinical practice statement (CPS) 2023. Obes Pillars. 2023.

[53] Hypertension related to obesity: pathogenesis, characteristics and factors for control. Int J Mol Sci. 2022;23(20):12305. https://doi.org/10.3390/ijms232012305