Original Article

# Development and Validation of the Accelerated Inflammatory-Metabolic Index (AIMI): A Composite Biomarker for Biochemical Assessment of Obesity-Associated Cardiometabolic Dysfunction



**Hayder Saleh[1], Majid Sirati-Sabet[2] and Zahra Shahsavari[2]**


## ABSTRACT

**Objective:** To develop and internally evaluate the accelerated inflammatory-metabolic index, integrating malondialdehyde, total antioxidant capacity, superoxide dismutase, interleukin-6, and homeostatic model assessment of insulin resistance and compare its diagnostic performance with that of its individual components across the obesity spectrum.

**Study Design:** A cross-sectional study

**Place and Duration of Study:** This study was conducted at the School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran from 1st March 2026 to 31st May 2026.

**Methods:** 150 adults in five age-matched groups (n = 30 each): non-obese, overweight, obese, severely obese, and trained athletes were enrolled. Accelerated inflammatory-metabolic index = [malondialdehyde x interleukin-6 x homeostatic model assessment of insulin resistance] ÷ [total antioxidant capacity × superoxide dismutase].

**Results:** Accelerated inflammatory-metabolic index increased progressively across groups ($F=187.4$, $p<0.0001$, $\eta^2=0.82$), from 0.65±0.19 in athletes to 24.71±8.43 in the severely obese group, and discriminated overweight from non-obese status with area under the curve = 0.976 (95% CI 0.935-1.000), numerically exceeding its strongest component, malondialdehyde (AUC = 0.939), and its weakest, homeostatic model assessment of insulin resistance (area under the curve = 0.693). Athlete accelerated inflammatory-metabolic index scores were significantly lower than non-obese controls (Cohen's d =0.91, $p<0.001$). Body mass index correlated more strongly than waist-to-hip ratio with every accelerated inflammatory-metabolic index component.

**Conclusions:** Accelerated inflammatory-metabolic index shows promising diagnostic performance for early metabolic deterioration and exercise-associated metabolic protection. External validation in independent, prospective cohorts is warranted before clinical use.


**Key Words:** Obesity, Oxidative stress, Insulin resistance, Systemic inflammation, Antioxidant capacity, Composite biomarker index, Cardiometabolic risk

**Citation of article: Saleh H, Sirati-Sabet M, Shahsavari Z. Development and Validation of the Accelerated Inflammatory-Metabolic Index (AIMI): A Composite Biomarker for Biochemical Assessment of Obesity-Associated Cardiometabolic Dysfunction. Med Forum 2026;37(8):43-48. doi:10.60110/medforum.370808.**

## INTRODUCTION

Obesity is a systemic metabolic disorder marked by concurrent oxidative stress, chronic inflammation, impaired antioxidant defense and insulin resistance.[1,2] Although these biological processes interact through interconnected molecular signalling pathways rather than proceeding independently, current clinical assessment relies predominantly on isolated biomarkers that fail to capture their integrated pathophysiology. Body mass index (BMI), the most widely applied anthropometric metric, captures neither adipose distribution nor any biochemical dimension of metabolic dysfunction[3], while single markers such as C-reactive protein (CRP), fasting glucose, or malondialdehyde (MDA) each address only one axis in isolation. The result is that individuals with normal fasting glucose but substantial insulin resistance, elevated oxidative burden, and subclinical inflammation remain undetected by standard clinical panels until disease is advanced.[4,5] Existing composite indices such as the triglyceride-glucose (TyG) index, the Visceral Adiposity Index (VAI), the Lipid Accumulation

[1.] M.Sc. Student / Associate Professor[2], Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Correspondence: Hayder Saleh, M.Sc. Student, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Contact No: 009647713875448
Email: haider_is@yahoo.co.uk

Received: June, 2026
Reviewed: July, 2026
Accepted: July, 2026

Product (LAP), and METS-IR predominantly integrate anthropometric and metabolic variables but do not account for oxidative stress or antioxidant defense, despite substantial evidence implicating these pathways in obesity-related metabolic dysfunction. Experimental evidence suggests that lipid peroxidation products such as MDA may activate NF-κB signalling, thereby promoting interleukin 6 (IL-6) expression and contributing to insulin resistance, and the resulting hyperinsulinaemia may in turn stimulate further peroxidative reactions.[6,7]

To address this gap, we introduce the Accelerated Inflammatory-Metabolic Index (AIMI), integrating oxidative injury (MDA), antioxidant capacity (TAC, SOD), inflammation (IL-6), and insulin resistance (HOMA-IR) - markers selected for biological relevance and strong association with obesity grade in this dataset (all $r \geq 0.80$, $p < 0.001$). A trained-athlete group was included as a physiological reference representing maximal metabolic protection, allowing AIMI to be evaluated across the full spectrum from protection to risk. The purposes were 1) to develop a composite biomarker (AIMI) integrating oxidative, antioxidant, inflammatory, and insulin-resistance axes; 2) to evaluate its diagnostic performance against individual biomarkers; and 3) to examine its association with anthropometric measures and training status.

# METHODS

A cross-sectional study was conducted at School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran from 1st March 2026 to 31st May 2026 vide letter IR.SBMU.MSP.REC.1404.775 dated 17th February 2026. A total of 150 adults in five age-matched groups (n = 30 each): non-obese (BMI 18.5-24.9 kg/m²), overweight (25.0-29.9), obese (30.0–39.9), severely obese (≥40.0), and trained athletes (BMI 18.5-24.9; ≥5 training sessions/week for ≥2 years) were enrolled. Demographic and lifestyle characteristics, including smoking status, medication use, comorbidities, and physical activity, were recorded for all individuals screened. Exclusion criteria included diabetes mellitus, cardiovascular disease, chronic inflammatory/autoimmune conditions, renal or hepatic impairment, use of agents affecting oxidative stress, inflammation, or lipid metabolism (statins, metformin, NSAIDs, corticosteroids), pregnancy, and active smoking. Participants fasted 10-12 hours before blood collection. The study was approved by the Institutional Ethics Committee and conducted in accordance with the Declaration of Helsinki (2013 revision); written informed consent was obtained from all participants.

Body mass index was calculated as weight (kg)/height (m)²; waist-hip ratio as waist÷hip circumference. Blood pressure was recorded twice in the seated position after 5 minutes of rest; the mean of two readings was used. Fasting venous blood was assayed in duplicate: MDA and SOD by ELISA; TAC by colorimetric FRAP assay; IL-6 and CRP by ELISA; fasting blood glucose (FBG) by the hexokinase method; insulin by electrochemiluminescence immunoassay; HOMA-IR = [insulin (mIU/mL) × FBG (mg/dL)] ÷ 405; lipid profile by standard enzymatic colorimetric methods. Five markers spanning the oxidative, antioxidant, inflammatory, and metabolic axes were selected for biological relevance and strong correlation with BMI: MDA, TAC (inverse), SOD (inverse), IL-6, and HOMA-IR.

Higher AIMI reflects greater pro-oxidant/inflammatory burden relative to antioxidant/metabolic protection. A multiplicative rather than additive structure was chosen because these axes are considered biologically synergistic. AIMI values were $\log_{10}$-transformed (log-AIMI) before statistical testing to normalise their right-skewed distribution.

The data was analyzed through SPSS-26. One-way ANOVA with LSD post-hoc testing compared groups; Pearson correlation assessed biomarker relationships; effect sizes were Cohen's d and $\eta^2$. Univariate logistic regression (BMI/WHR excluded as they define the groups) and ROC analysis (95% CIs and cutoffs via percentile bootstrap, 3,000 resamples) evaluated diagnostic performance. $\alpha = 0.05$, two-tailed.

# RESULTS

Groups were age-matched ($F = 0.72$, $p = 0.58$). BMI ranged from 21.94±1.57 (non-obese) to 47.08 ± 8.06 kg/m² (severely obese); WHR rose from 0.803 ± 0.06 to 0.946±0.11, with athlete WHR (0.824±0.06) comparable to controls. All groups recorded normal mean systolic BP (<120 mmHg) [Table 1]. All twelve biomarkers differed significantly across groups (all $p < 0.0001$), generally following a dose-dependent BMI gradient, except IL-6, CRP, and TAC, which showed partial attenuation in the severely obese group (Table 2). HOMA-IR, MDA, CRP, and IL-6 were mutually intercorrelated ($r > 0.74$, $p < 0.001$); TAC–MDA showed the strongest inverse correlation ($r = -0.891$). BMI correlated more strongly than WHR with every AIMI component (advantage 0.05–0.30), contrary to the initial expectation that a central-adiposity measure would outperform a global one (Table 3).

Within-group analyses confirmed that FBG–HOMA-IR (strongest in the obese group, $r = 0.87$) and CRP–IL-6 associations (overweight $r = 0.44$; obese $r = 0.44$) persisted even within narrow BMI bands, indicating these relationships are not simply artifacts of pooling groups with different adiposity (Figs. 1-3). Log-AIMI increased progressively across groups ($F=187.4$, $p<0.0001$, $\eta^2=0.82$), from 0.65±0.19 (athletes) to 24.71±8.43 (severely obese) - a ~38-fold difference. Athlete AIMI was significantly below non-obese controls (Cohen's $d = 0.91$, $p<0.001$) [Table 4].

**Table No. 1: Participant characteristics, NS = not significant**

| Parameter | Non-Obese | Overweight | Obese | Severely Obese | Athletes | p-value |
|---|---|---|---|---|---|---|
| Age (years) | 35.47±15.29 | 37.10±12.20 | 39.56±15.63 | 36.37±13.96 | 32.50±11.19 | 0.581 NS |
| BMI (kg/m²) | 21.94±1.57 | 27.37±1.33 | 34.02±2.56 | 47.08±8.06 | 22.12±1.94 | <0.0001 |
| WHR | 0.803±0.06 | 0.848±0.07 | 0.905±0.08 | 0.946±0.11 | 0.824±0.06 | <0.0001 |
| Systolic BP | 109.47±6.18 | 116.86±4.54 | 117.43±2.75 | 114.90±5.29 | 117.00±3.73 | <0.0001 |

**Table No. 2: Biochemical biomarker values across groups, *Partial attenuation in the severely obese group relative to the obese group. Cohen's d between non-obese and severely obese groups; TG = triglycerides**

| Biomarker | Non-Obese | Overweight | Obese | Severely Obese | Athletes | Cohen's d |
|---|---|---|---|---|---|---|
| FBG (mg/dL) | 89.42±2.97 | 90.34±3.89 | 103.65±12.47 | 112.79±14.78 | 86.39±4.18 | 2.01 |
| HOMA-IR | 1.466±0.20 | 1.617±0.27 | 2.913±1.38 | 7.45±2.29 | 1.516±0.25 | 2.89 |
| MDA (nmol/mL) | 1.219±0.14 | 1.630±0.21 | 3.879±0.57 | 4.018±1.01 | 1.280±0.18 | 4.63 |
| TAC (mmol/L) | 1.596±0.08 | 1.384±0.13 | 0.943±0.12 | 1.224±0.21* | 1.623±0.12 | 6.82 |
| SOD (U/mL) | 5.35±0.29 | 4.87±0.38 | 3.27±0.50 | 2.01±0.64 | 5.24±0.37 | 5.48 |
| CRP (mg/dL) | 0.840±0.37 | 1.838±0.56 | 10.22±3.17 | 9.05±3.31* | 0.927±0.38 | 3.71 |
| IL-6 (pg/mL) | 2.48±0.71 | 3.73±1.03 | 11.81±3.72 | 7.54±2.59* | 2.25±0.87 | 2.94 |
| Total Chol (mg/dL) | 176.41±13.34 | 184.94±13.11 | 222.66±25.50 | 234.01±22.73 | 178.54±12.38 | 2.61 |
| TG (mg/dL) | 83.98±15.59 | 113.62±18.08 | 237.75±60.64 | 223.10±48.19 | 81.35±19.61 | 3.02 |
| HDL-C (mg/dL) | 61.87±4.59 | 56.58±5.69 | 40.27±5.53 | 46.66±5.79 | 61.05±4.02 | 3.84 |
| LDL-C (mg/dL) | 110.36±9.51 | 110.28±10.77 | 151.26±20.35 | 148.89±19.81 | 105.31±8.54 | 2.12 |

**Table No. 3: Pearson correlation matrix of AIMI components and BMI (n = 150) ** p < 0.001 (two-tailed)**

| | HOMA-IR | MDA | TAC | SOD | IL-6 | BMI |
|---|---|---|---|---|---|---|
| HOMA-IR | 1.000 | 0.812** | −0.743** | −0.762** | 0.741** | 0.781** |
| MDA | 0.812** | 1.000 | −0.891** | −0.814** | 0.796** | 0.758** |
| TAC | −0.743** | −0.891** | 1.000 | 0.867** | −0.743** | −0.583** |
| SOD | −0.762** | −0.814** | 0.867** | 1.000 | −0.718** | −0.865** |
| IL-6 | 0.741** | 0.796** | −0.743** | −0.718** | 1.000 | 0.508** |

**Table No. 4: AIMI scores by group (ANOVA p<0.0001; $\eta^2 = 0.82$)**

| Group | Raw AIMI (Mean±SD) | Log-AIMI (Mean±SD) | Risk Category |
|---|---|---|---|
| Athletes | 0.65±0.19 | −0.19±0.12 | Below reference |
| Non-Obese (Control) | 2.01±0.61 | 0.30±0.13 | Reference |
| Overweight | 3.87±0.94 | 0.59±0.11 | Mild risk |
| Obese | 12.43±3.18 | 1.09±0.11 | High risk |
| Severely Obese | 24.71±8.43 | 1.39±0.14 | Very high risk |

**Table No. 5: ROC analysis: AIMI vs. individual biomarker components (overweight vs. non-obese, n = 30/group)**

| Biomarker/Index | AUC | 95% CI | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|
| AIMI (composite) | 0.976 | 0.936–1.000 | 90.0 | 100.0 |
| MDA | 0.939 | 0.869–0.990 | 80.0 | 100.0 |
| CRP | 0.933 | 0.863–0.984 | 86.7 | 86.7 |
| TAC (inverse) | 0.887 | 0.788–0.963 | 76.7 | 96.7 |
| IL-6 | 0.837 | 0.722–0.927 | 73.3 | 83.3 |
| SOD (inverse) | 0.826 | 0.711–0.918 | 66.7 | 90.0 |
| HOMA-IR | 0.693 | 0.554–0.823 | 66.7 | 76.7 |

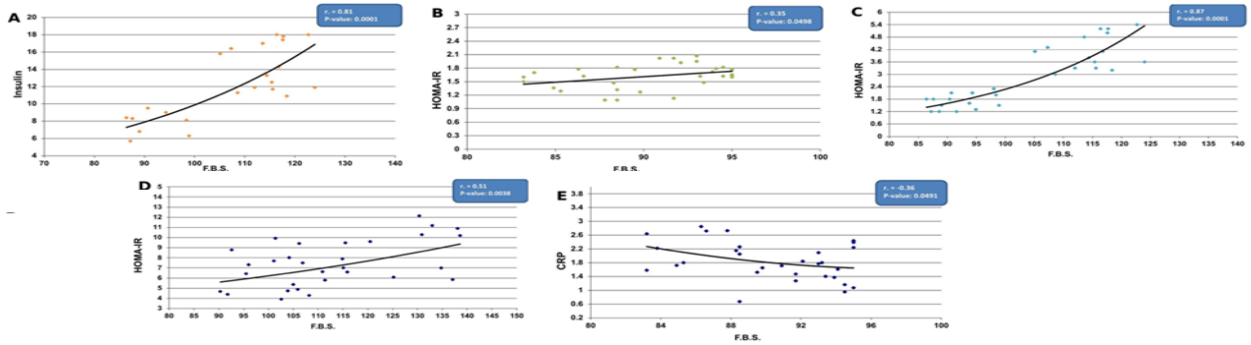


**Figure No. 1: Relationship between fasting blood glucose (FBG) and glycaemic/insulin-resistance markers within individual study groups: (A) FBG vs insulin, obese group; (B) FBG vs. HOMA-IR, overweight group; (C) FBG vs. HOMA-IR, obese group; (D) FBG vs HOMA-IR, severely obese group; (E) FBG vs CRP, overweight group**

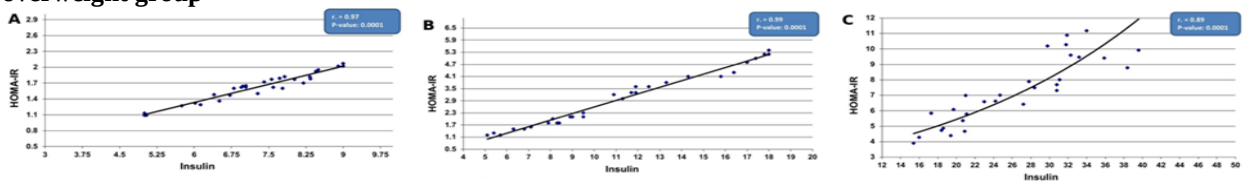


**Figure No. 2: Relationship between insulin and HOMA-IR within individual study groups: (A) overweight; (B) obese; (C) severely obese**

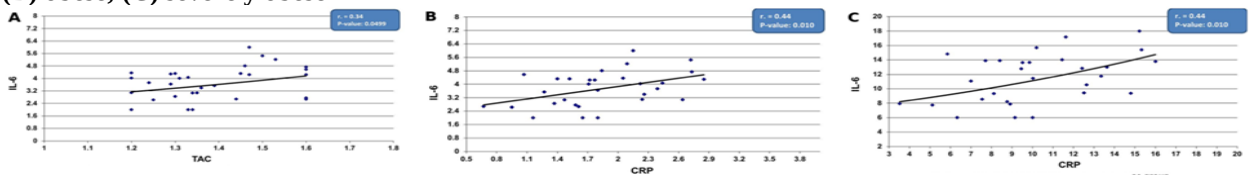


**Figure No. 3: Relationship between oxidative/inflammatory markers and IL-6 within individual study groups: (A) TAC vs IL-6, overweight; (B) CRP vs. IL-6, overweight; (C) CRP vs. IL-6, obese**

An extreme-phenotype comparison (obese and severely obese vs. non-obese and athletes) was not used because it produced near-ceiling discrimination for most markers and an AUC of 1.000 for BMI, since these groups are themselves defined by BMI thresholds; testing whether BMI predicts a BMI-defined grouping is circular and was dropped rather than reported as a finding, and WHR was excluded for the analogous reason. AIMI achieved AUC=0.976 (95% CI 0.935-1.000; sensitivity 90.0%, specificity 100.0%; Table 5), correctly classifying 57 of 60 participants, and numerically exceeded all individual components; the AIMI-vs-MDA difference was not statistically significant (bootstrap 95% CI: -0.028 to 0.114) [Table 5]. Because BMI and WHR define the groups modelled, neither was entered as a predictor. Each component was independently associated with overweight status per 1-SD increase: MDA (OR = 9.95, 95% CI 5.81-18.19), IL-6 (OR =4.23, 2.48-8.27), HOMA-IR (OR = 1.82, 1.11-3.34), TAC (OR = 0.14, 0.08–0.23), and SOD (OR = 0.25, 0.13-0.41); all 95% CIs excluded 1. A joint multivariable model could not be fitted reliably at this sample size due to quasi-complete separation.

# DISCUSSION

The biochemical perturbations of obesity are mechanistically interconnected rather than independent: HOMA-IR, MDA, CRP, and IL-6 were mutually intercorrelated (r>0.74), and TAC–MDA showed a strong inverse relationship (r = −0.891), consistent with MDA-driven NF-κB activation promoting IL-6 expression and insulin resistance while depleting antioxidant reserves.[1] MDA forms adducts with IRS-1 that impair insulin receptor signalling, contributing directly to HOMA-IR elevation[8,9], while the NLRP3 inflammasome links oxidative and inflammatory injury at a single molecular node, amplifying IL-6 production and impairing β-cell function.[7] AIMI's multiplicative ratio structure encodes this synergy directly: as obesity advances, the numerator (MDA×IL-6×HOMA-IR) expands while the denominator (TAC×SOD) contracts, producing a 38-fold AIMI differential between athletes and severely obese participants versus a 3.3-fold difference for MDA alone.

Body mass index predicted all five AIMI components more strongly than WHR (advantage 0.05–0.30), suggesting AIMI reflects total systemic adiposity burden rather than fat distribution specifically. This supports using BMI, already routinely collected, as the primary anthropometric trigger for AIMI screening, though this interpretation requires confirmation since visceral adiposity was not directly measured.

Partial attenuation of IL-6, CRP, and TAC in the severely obese group may reflect chronic IL-6 receptor downregulation under sustained cytokine overexposure, or a compensatory Nrf2-driven antioxidant response as a hormetic reaction to extreme oxidative burden[10,11], though unmeasured confounders such as medication use (particularly statins, which reduce CRP by 25-50%) and dietary antioxidant intake cannot be excluded. Despite this component-level attenuation, mean AIMI remained substantially higher in the severely obese group (24.71±8.43) than in the obese group (12.43±3.18), because continued SOD suppression and HOMA-IR elevation dominate the denominator and numerator respectively.

Athletes recorded AIMI significantly below the non-obese control reference (Cohen's d =0.91, $p<0.001$) while maintaining BMI values comparable to controls, reflecting coordinated physiological adaptations: Nrf2-driven upregulation of Mn-SOD and glutathione peroxidase raises the denominator; reduced basal ROS generation lowers MDA; diminished visceral adiposity attenuates IL-6 secretion; and AMPK-mediated GLUT-4 translocation normalises HOMA-IR. Notably, all five individual AIMI components showed only athlete, control equivalence ($p>0.05$) rather than athlete superiority; AIMI's ratio structure, by multiplying these small individual advantages, converts a pattern of statistical non-difference into a quantifiable index advantage, a mathematical property of composite ratio indices that should be interpreted with appropriate caution in future applications.[12]

Accelerated inflammatory-metabolic index has four potential clinical applications distinct from existing individual markers. For early screening, AIMI was elevated in the overweight group despite near-normal FBG, indicating it detects metabolic deterioration before glucose-based tests become informative. For obesity phenotyping, AIMI integrates the dimensions distinguishing metabolically healthy from unhealthy obese phenotypes. For treatment monitoring, its numerator and denominator components are expected to respond to interventions at different kinetics, allowing serial measurement to track multi-domain recovery. For exercise dose-response research, the athlete group's below-reference AIMI offers a quantitative target for training prescriptions. This rationale for multi-marker profiling extends to other conditions, such as neurochemical panels in methamphetamine use disorder[13,14], reinforcing that composite indices can capture information no single marker provides alone.

Unlike existing composite indices (TyG, LAP, VAI), which rely solely on lipid/glucose variables[15,16], AIMI incorporates the redox dimension, which correlated strongly with insulin resistance (r=0.812) and TAC (r=−0.891) in this dataset. Head-to-head comparison with these established indices in the same cohort is a logical next step for establishing AIMI's incremental value.

# CONCLUSION

Accelerated inflammatory-metabolic index detected meaningful metabolic deterioration before FBG or lipid parameters exceeded normal thresholds, maintained directional validity despite partial component attenuation in severely obese participants, and distinguished athletes' exercise-associated metabolic protection (Cohen's d = 0.91), a pattern not detectable from individual markers alone. Before clinical application, AIMI requires prospective validation in larger, diverse cohorts with documented medication use and dietary intake, and direct comparison with TyG, LAP, and VAI. Subject to such validation, AIMI may represent a promising, mechanistically grounded index for cardiometabolic risk assessment, treatment monitoring, and exercise evaluation in obesity.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design or acquisition of analysis or interpretation of data: | Hayder Saleh, Majid Sirati-Sabet |
| Drafting or Revising Critically: | Hayder Saleh, Zahra Shahsavari |
| Final Approval of version: | All the above authors |
| Agreement to accountable for all aspects of work: | All the above authors |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**Source of Funding:** None

**Ethical Approval:** No. SBMU.MSP.REC.1404.775 Dated 17.02.2026

# REFERENCES

1. Hotamisligil GS. Inflammation and metabolic disorders. Nature 2026; 444(7121): 860-67.
2. Furukawa S, Fujita T, Shimabukuro M, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest 2004; 114(12): 1752-61.
3. Despres JP, Lemieux I, Bergeron J, et al. (2008). Abdominal obesity and the metabolic syndrome. Arterioscler Thromb Vasc Biol 2008; 28(6): 1039-49.
4. DeFronzo RA, Ferrannini E, Groop L, et al. Type 2 diabetes mellitus. Nature Reviews Disease Primers 2013; 1: 15019.
5. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease. Circulation 2003; 107(3): 363-9.
6. Samuel VT, Shulman GI. Mechanisms for insulin resistance. Cell 2012; 148(5): 852-71.

7. Vandanmagsar B, Youm YH, Ravussin A, et al. The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance. Nat Med 2011; 17(2): 179-88.
8. Del Rio D, Stewart AJ, Pellegrini N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress. Nutr Metab Cardiovasc Dis 2005; 15(4): 316-28.
9. Kern PA, Ranganathan S, Li C, Wood L, Ranganathan G. Adipose tissue TNF and IL-6 expression in human obesity and insulin resistance. Am J Physiol Endocrinol Metab 2001; 280(5): E745-51.
10. Merry TL, Ristow M. Nrf2 mediates exercise-induced mitochondrial biogenesis and antioxidant response in mice. J Physiol 2016; 594(18): 5195-5207.
11. Hosmer DW, Lemeshow S. Applied Logistic Regression. 2nd ed. John Wiley & Sons; 2000.p.55.
12. American Heart Association/American College of Cardiology. 2017 guideline for high blood pressure in adults. J Am Coll Cardiol 2017; 71(19): e127-248.
13. Talib NH, Majeed MJ, Hussein MM. Beta-endorphin and serotonin levels in individuals with methamphetamine use disorder. J Faculty Med Baghdad 2025; 58.
14. Reaven G. The metabolic syndrome or the insulin resistance syndrome? Endocrinol Metab Clin North Am 2005;33(2): 283-303.
15. American Diabetes Association. Standards of care in diabetes -2023. Diabetes Care 2023; 46(Suppl. 1): S1-267.
16. DeFronzo RA, Ferrannini E, Groop L, et al. Type 2 diabetes mellitus. Nat Rev Dis Primers 2013;1: 15019.