# The Role of Mitochondrial Dysfunction Biomarkers in Metabolic Syndrome


## Abstract

**Aims:** This study aimed to evaluate biomarkers of mitochondrial dysfunction, oxidative stress, antioxidant defense, insulin resistance, and inflammation in patients with metabolic syndrome and to determine their associations with metabolic-syndrome characteristics compared with healthy controls.

**Materials & Methods:** A prospective case-control study included 128 participants recruited from Baghdad Central Hospital, Iraq: 64 patients with metabolic syndrome, predominantly characterized by insulin resistance, and 64 healthy controls. Participants were randomly selected according to predefined eligibility criteria and classified by health status. Clinical and biochemical assessments included body mass index (BMI), waist circumference, systolic and diastolic blood pressure, fasting glucose, HbA1c, fasting insulin, HOMA-IR, triglycerides, HDL cholesterol, LDL cholesterol, total cholesterol, and biomarkers related to mitochondrial dysfunction, oxidative stress, antioxidant defense, and inflammation. Case-control comparisons and five-group Welch ANOVA were performed to evaluate differences among study groups.

**Findings:** Case-control analyses showed significant differences in 22 measured outcomes, while age and catalase were not significantly different. The largest standardized differences were observed for metabolic-syndrome component count, thiobarbituric acid-reactive substances (TBARS), fasting insulin, HOMA-IR, fasting glucose, BMI, HbA1c, and waist circumference. Five-group Welch ANOVA similarly identified significant phenotype differences in 22 outcomes, with age and catalase remaining non-significant. The strongest phenotype effects, based on eta-squared values, involved metabolic-syndrome component count, TBARS, fasting insulin, HOMA-IR, fasting glucose, HbA1c, BMI, and triglycerides.

**Conclusion:** Metabolic syndrome is associated with alterations in biomarkers of oxidative stress, inflammation, and insulin resistance, supporting their relevance to metabolic dysfunction and disease characterization.



## Keywords

Metabolic Syndrome [https://www.ncbi.nlm.nih.gov/mesh/68024821];
Mitochondrial Dysfunction [https://www.ncbi.nlm.nih.gov/mesh/68028361];
Oxidative Stress [https://www.ncbi.nlm.nih.gov/mesh/68018384];
Insulin Resistance [https://www.ncbi.nlm.nih.gov/mesh/68007333];
Inflammation [https://www.ncbi.nlm.nih.gov/mesh/68007249];
Biomarkers [https://www.ncbi.nlm.nih.gov/mesh/68015415]



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## Introduction

Metabolic syndrome, or metabolic dysfunction syndrome, is one of the most common syndromes associated with five medical risk factors, including high blood pressure, excessive fats in the body, and high blood sugar [1-4], which may be due to insulin resistance. These main medical risk factors can progress into metabolic syndrome. The prevalence of metabolic syndrome worldwide is increasing to more than 11%, and in the East region, it is more than 16% of total metabolic disorders in the region (Figure 1).

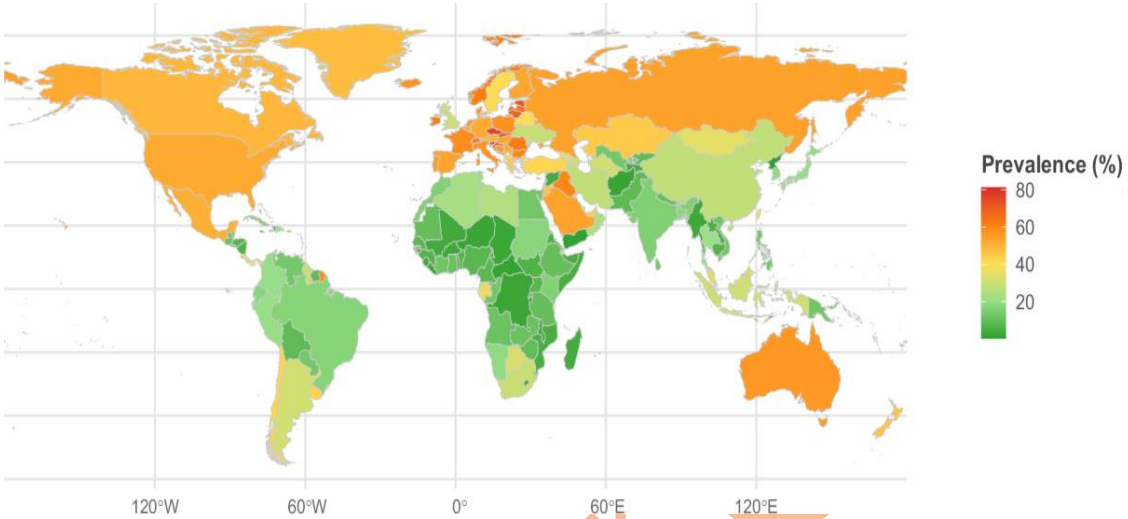


**Figure 1.** Metabolic syndrome prevalence trends (2000 to 2024) [4]

A number of interconnected cardiometabolic disorders, such as increased body obesity, raised blood pressure, dysregulated blood glucose, and aberrant lipid metabolism, coexist in metabolic syndrome, a complicated metabolic illness. These metabolic abnormalities may gradually raise the risk of cardiovascular disease, stroke, and type 2 diabetes mellitus and are strongly linked to insulin resistance. Due to the growing prevalence of metabolic syndrome worldwide, early detection and characterization of the condition are crucial for both clinical and public health. According to recent data, the prevalence of metabolic syndrome has been rising globally, with significant regional and population variations [5-9].

Numerous interrelated factors, including as age, dietary habits, physical activity, and metabolic status, affect the onset and course of metabolic syndrome. Disturbances in glucose and lipid metabolism are directly linked to insulin resistance, which is regarded as a key component of the syndrome. The molecular causes driving metabolic dysfunction, particularly oxidative stress, inflammation, and mitochondrial abnormalities, have received more attention in addition to these traditional clinical features [10-12].

Mitochondria are essential for both metabolic equilibrium and the synthesis of cellular energy. Changes in mitochondrial activity may be linked to obesity and metabolic syndrome as well as reduced cellular metabolism. Disturbances in mitochondrial DNA and other cellular functions have been connected to mitochondrial dysfunction, and oxidative stress may exacerbate metabolic problems by producing too many reactive oxygen species. Therefore, a number of biomarkers, such as malondialdehyde (MDA), thiobarbituric acid-reactive substances (TBARS), superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), and reduced glutathione (GSH), have been studied to describe oxidative imbalance and compromised antioxidant defense [14-16].

Insulin resistance and persistent low-grade inflammation are also intimately linked to oxidative damage. While inflammatory processes may exacerbate insulin resistance and metabolic dysfunction, increased oxidative damage may hinder cellular signaling and metabolic regulation. Thus, a more comprehensive picture of the biochemical changes linked to metabolic syndrome may be obtained by concurrently evaluating metabolic, oxidative-stress, antioxidant, and inflammatory indicators [12, 13, 16].

Despite the increasing awareness of mitochondrial dysfunction, oxidative stress, and inflammation as components of metabolic syndrome, the interactions among these biomarkers and conventional

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metabolic indicators require more exploration in different patient populations. Thus, among patients with metabolic syndrome and healthy controls, the current study sought to assess specific biomarkers linked to mitochondrial dysfunction, oxidative stress, antioxidant defense, insulin resistance, and inflammation. Additionally, the study looked at how these indicators differed between the two groups and investigated how they related to the biochemical and clinical features of metabolic syndrome.

## Materials and Methods

128 people were included in a case-control prospective study design (64 patients with various metabolic disorders, primarily insulin resistance, and 64 as healthy controls).

The biomarkers for mitochondrial dysfunction, oxidative stress, antioxidant defense, insulin resistance, and inflammation were examined in this study.

**Recruitment**

From January 2025 to March 2026, this study was carried out at Baghdad Central Hospital in Iraq. Eligible volunteers were found and evaluated over this time in accordance with predetermined inclusion and exclusion criteria. Participants were divided into metabolic syndrome cases and healthy controls based on their clinical and biochemical traits after being chosen at random from the available population. After being fully informed about the study's objectives, participants were asked to take part. G*Power software was used to determine the sample size based on the estimated effect size, predetermined statistical parameters, and a 95% confidence interval. There were 128 persons in the final sample, 64 of whom had metabolic syndrome and 64 of whom were healthy controls. After recruiting eligible participants using a random selection process, the participants were stratified based on their metabolic syndrome status.

**Sample collection**

A peripheral blood sample was obtained from all participants at a 12-hour fasting level; All blood samples were put into an EDTA tube before centrifugation at 5000 x g for 10 minutes.

**Biomarkers assessment**

The oxidative stress biomarkers of malondialdehyde (MDA) and lipid peroxidase were investigated according to the guidelines of Alberti *et al.* [11], Awadallah *et al.* [12], and Carballo-Casla *et al.* [13]. Also, Superoxide dismutase (SOD), Catalase (CAT), Glutathione peroxidase (GPx), and reduced glutathione (GSH) were investigated as antioxidant biomarkers according to the procedures of Kim *et al.* [14], Matthews *et al.* [15], and Vona *et al.* [16]. Also, fasting plasma glucose, fasting serum insulin, Glycated hemoglobin (HbA1c), HOMA-IR, Interleukin-6 (IL-6), Tumor necrosis factor-alpha (TNF-α), CRP, and ESR were measured in all samples as diabetes and inflammatory markers [17, 18].

Metabolic syndrome measurements included standard clinical and biochemical components of metabolic syndrome, which should also be measured, such as Body mass index (BMI), Systolic and diastolic blood pressure, Triglycerides, HDL and LDL cholesterol, and Total cholesterol [19-21].

**Ethical approval**

IRB approval was obtained from the University of Baghdad, Iraq, with IRB number 2369-c2026. Confidentiality was assured to all participants, as well as the single-blind trial was achieved with total anonymity for all participants during the study.

**Statistical analysis**

All data were analyzed at the level of significance ($p<0.05$) using the R program for analysis and data visualization using several R packages such as ggplot2.

## Findings

This case-control prospective study design was performed on 128 participants (64 patients with different metabolic syndromes, mainly with insulin resistance, and 64 as healthy controls).

Cases demonstrated an adverse anthropometric and cardiometabolic profile compared with healthy controls. The case group showed higher body mass index, waist circumference, systolic and diastolic blood pressure, triglycerides, LDL cholesterol, and total cholesterol, together with lower HDL cholesterol.

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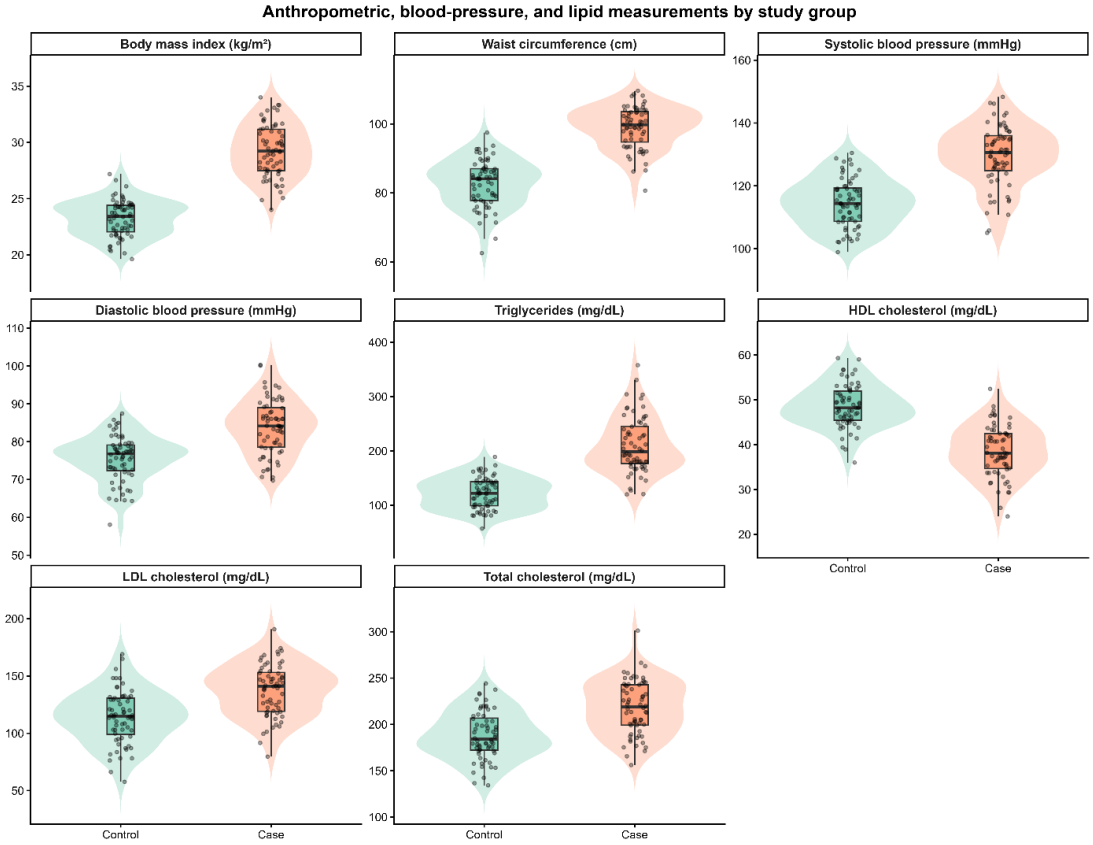


**Figure 2.** Anthropometric, blood-pressure, and lipid measurements in cases and healthy controls. Violin plots illustrate the distribution density of each measurement, embedded boxplots represent the median and interquartile range, and individual points represent participants. Green indicates healthy controls, and orange indicates cases with metabolic syndrome or insulin resistance **(It's not referenced in the text)**

Fasting plasma glucose, fasting insulin, HOMA-IR, HbA1c, and metabolic syndrome component counts were significantly higher in the case group than in the control group, indicating significant derangements of glucose regulation and insulin sensitivity in the case group.

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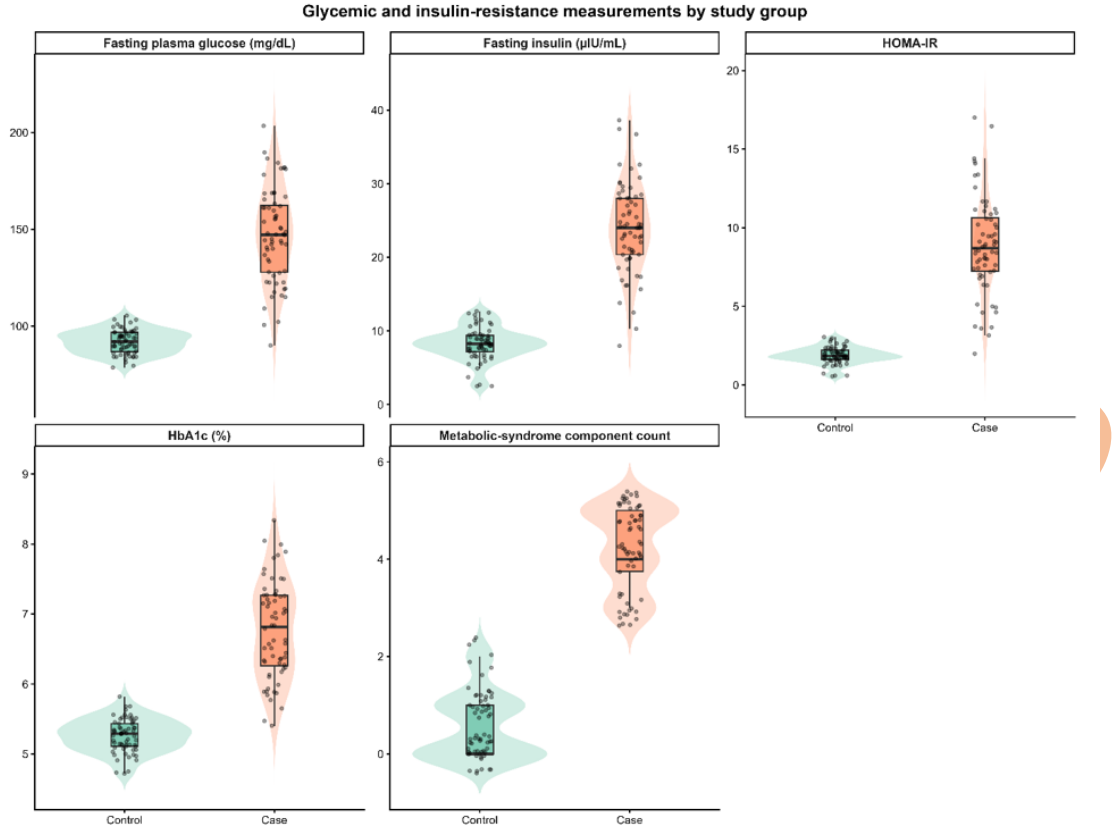


**Figure 3.** Glycemia and insulin resistance parameters in cases and healthy controls. Violin plots with embedded boxplots and individual observations are presented for distributions of fasting plasma glucose, fasting insulin, HOMA-IR, HbA1c, and metabolic-syndrome component count. Orange=cases, green=control **(It's not referenced in the text)**

There was evidence of enhanced oxidative stress in the cases, which was indicated by greater amounts of malondialdehyde and TBARS among the cases. There was a tendency for antioxidant-defense indicators, specifically superoxide dismutase, glutathione peroxidase, and reduced glutathione, to be lower among the patients, but catalase showed a significant amount of overlap between the groups.

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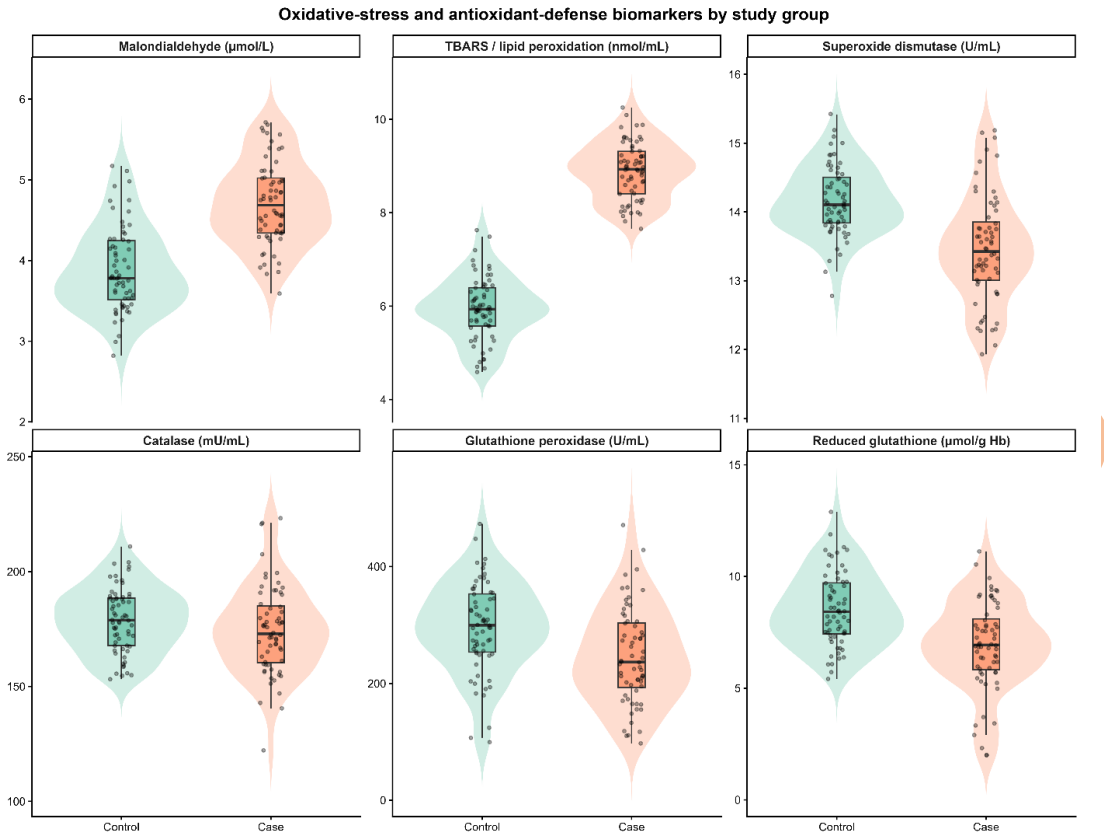


**Figure 4.** Biomarkers of oxidative stress and antioxidant defense in the patients and healthy controls. The panels illustrate the distribution of malondialdehyde, TBARS, superoxide dismutase, catalase, glutathione peroxidase, and reduced glutathione. Violin plots illustrate distribution density; Boxplots show median and interquartile range, and dots depict individual participation **(It's not referenced in the text)**

In general, the inflammatory biomarkers were substantially greater in patients than in controls. The best separation between groups was observed for IL-6 and TNF-α. CRP and ESR showed higher mean values and higher dispersion in patients.

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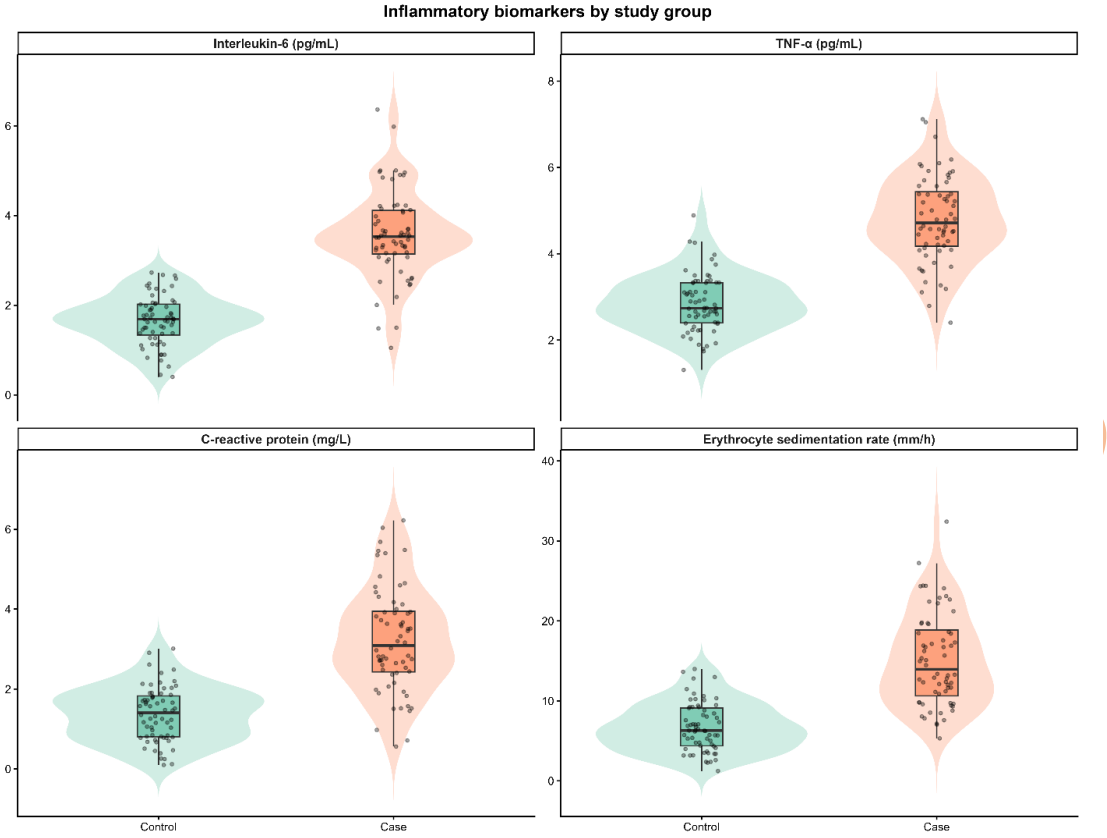


**Figure 5.** Inflammatory biomarkers in patients and healthy controls. Figure 2. Violin plots with embedded boxplots and individual participant observations for distributions of interleukin-6, TNF-α, C-reactive protein, and erythrocyte sedimentation rate. Green controlled by Orange (cases) **(It's not referenced in the text)**

The forest plot shows the size and direction of standardized case-control differences. Metabolic-syndrome component count, TBARS, fasting insulin, HOMA-IR, fasting glucose, BMI, and HbA1c showed the greatest favorable benefits. HDL cholesterol and certain indicators of antioxidant activity revealed a deleterious effect, with lower levels among patients.

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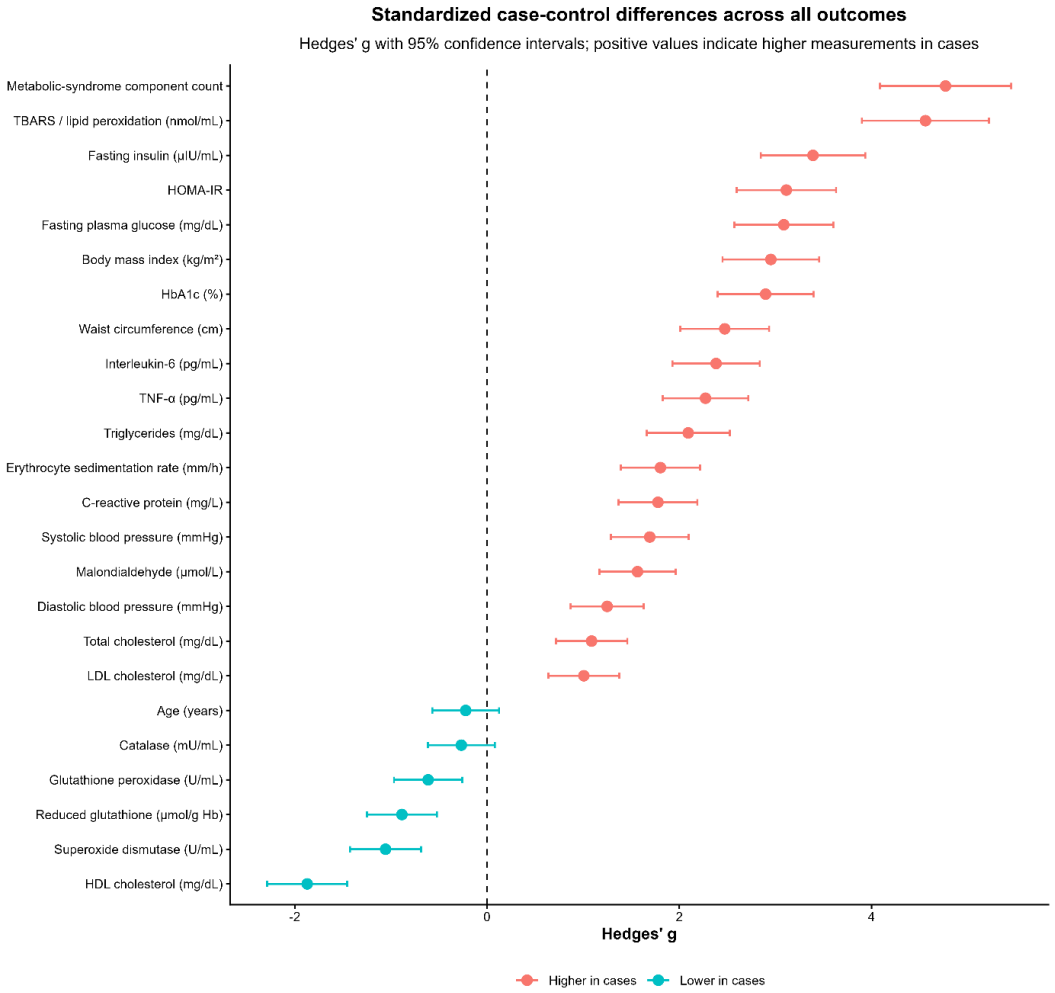


**Figure 6.** Standardized case-control differences for all clinical and biochemical outcomes assessed. Points are Hedges' g and horizontal lines are 95% confidence intervals. Positive numbers indicate greater readings in cases; negative values indicate lower measurements in cases. The dashed vertical line indicates no difference between groups as normal **(It's not referenced in the text)**

The correlation matrix identified clustering of metabolic, glycemic, oxidative-stress, and inflammatory measures that were largely positively associated. HDL cholesterol and antioxidant defense indicators exhibited the greatest negative associations with an unfavorable metabolic and inflammatory profile.

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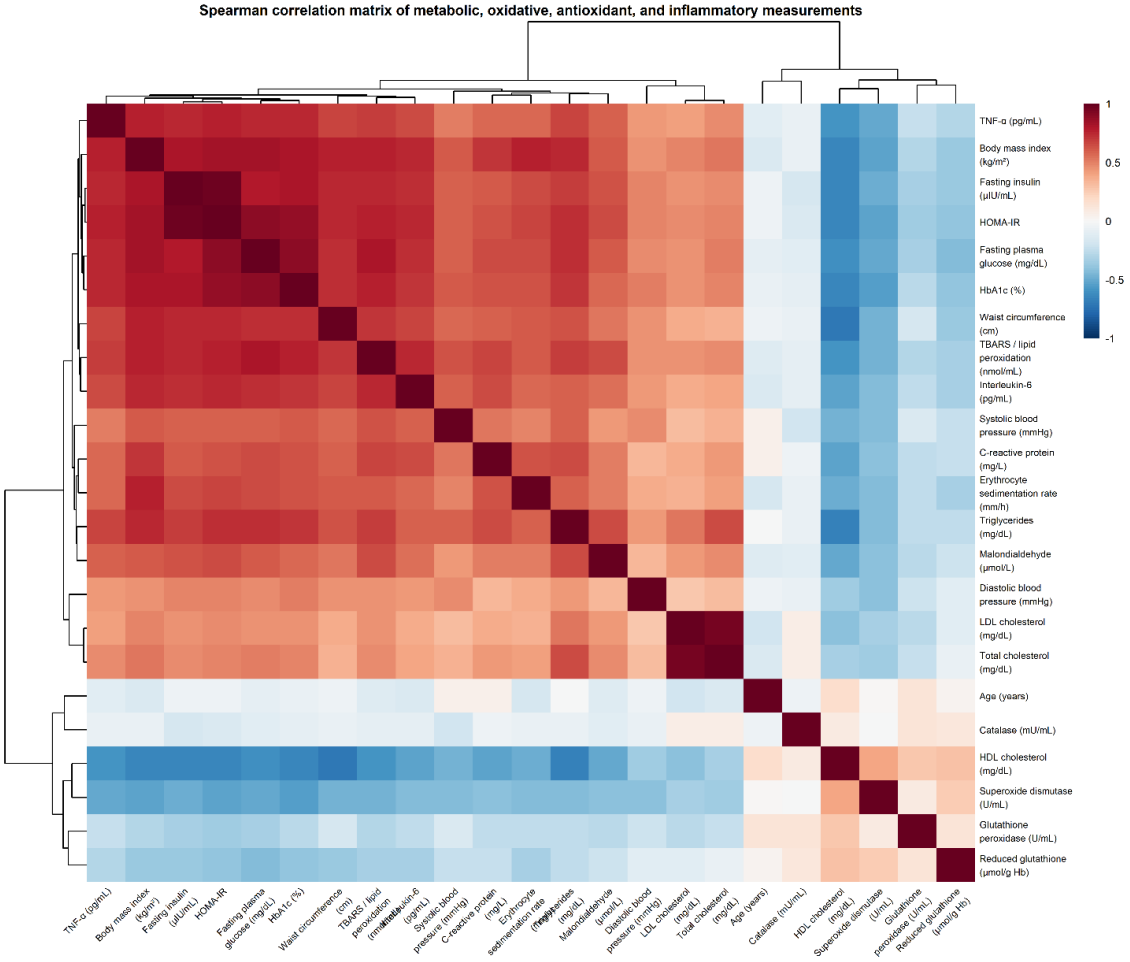


**Figure 7.** Spearman correlation matrix of metabolic, oxidative stress, antioxidant, and inflammatory markers. Shading of red denotes positive correlations, shading of blue indicates negative correlations, and the stronger the link, the more intense the hue. Hierarchical clustering dendrograms group variables by similar correlation patterns **(It's not referenced in the text)**

Principal component analysis demonstrated a distinct multivariate separation between patients and controls mainly along the first principal component, which explained 55.3% of the total variance. The case group was more scattered, indicating more variability of the overall biomarker profile.

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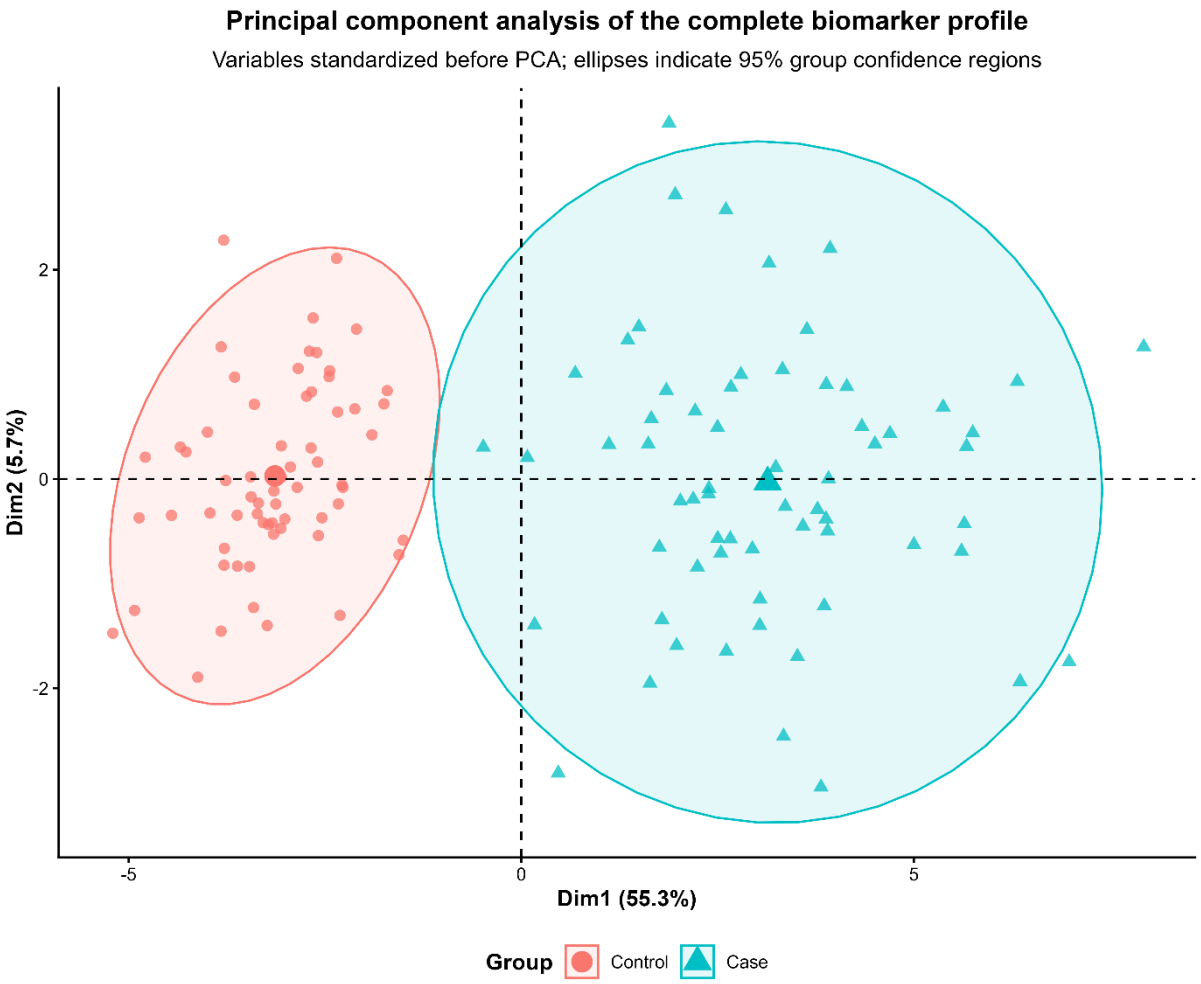


**Figure 8.** Principal component analysis of the whole biomarker profile in patients and healthy controls. Each point represents one subject on standardized clinical and biochemical measures. The first and second main components explained 55.3% and 5.7% of the variation, respectively. Ellipses are the 95% confidence area of each group **(It's not referenced in the text)**

HOMA-IR demonstrated a positive correlation with inflammatory markers; Like interleukin-6, TNF-α, CRP, ESR, and oxidative-stress markers; Like malondialdehyde and TBARS. The results are consistent with increased insulin resistance being associated with increased systemic inflammation and oxidative stress in this dataset.

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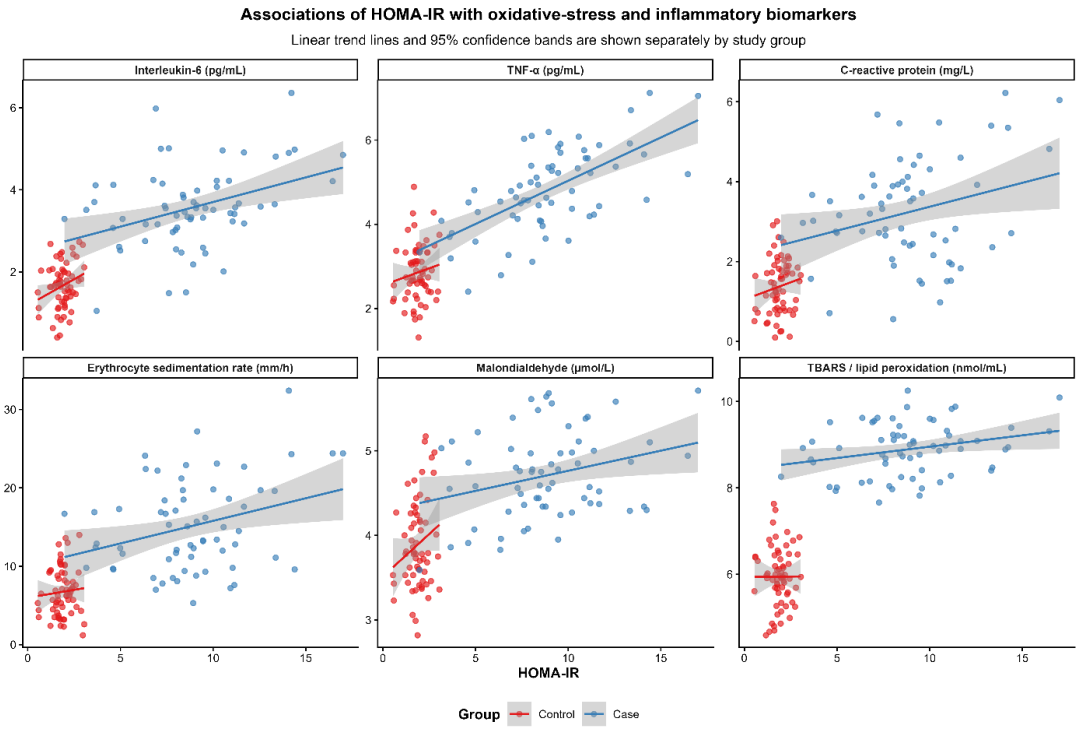


**Figure 9.** HOMA-IR and indicators of oxidative stress and inflammation Figure 2. Scatterplots of individual values of interleukin-6, TNF-α, C-reactive protein, erythrocyte sedimentation rate, malondialdehyde, and TBARS. Controls and patients are presented with independent linear regression lines with 95% confidence bands **(It's not referenced in the text)**

HOMA-IR, fasting glucose, fasting insulin, HbA1c, and TBARS performed exceptionally well in terms of discriminating between cases and controls, according to the results of the ROC analysis. CRP exhibited relatively reduced, but still strong, discriminatory ability in the synthetic sample, but TBARS revealed complete separation in the synthetic dataset.

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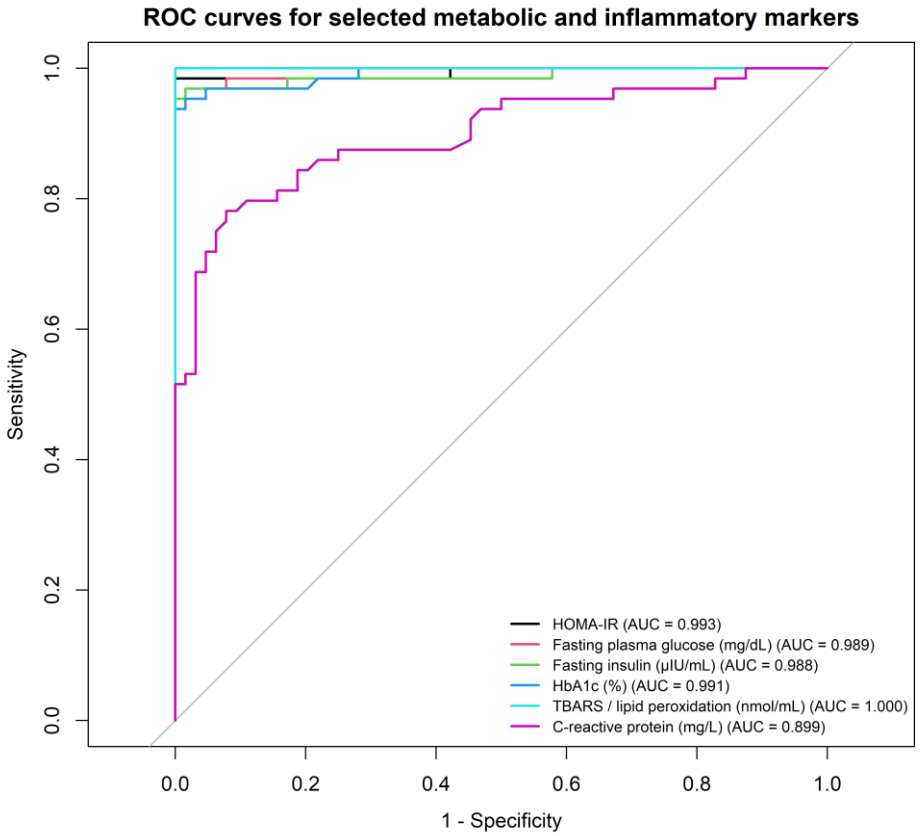


**Figure 10.** Receiver operating characteristic curves for selected metabolic and inflammatory markers. Curves show the sensitivity and 1–specificity of HOMA-IR, fasting plasma glucose, fasting insulin, HbA1c, TBARS, and C-reactive protein for distinguishing cases from healthy controls. The corresponding areas under the curve were 0.993, 0.989, 0.988, 0.991, 1.000, and 0.899, respectively. The diagonal line represents performance expected by chance **(It's not referenced in the text)**

Both classical one-way ANOVA and Welch ANOVA were calculated. The tables below report Welch ANOVA because several outcomes showed unequal variances. Benjamini-Hochberg FDR correction was applied across the 24 outcomes (Tables 1 & 2).

**Table 1.** Unpaired case-control results

| Variable | Control (mean±SD) | Case (mean±SD) | t | Raw p | FDR q | Hedges' g |
|---|---|---|---|---|---|---|
| **Age** | 46.14±6.98 | 44.45±8.10 | −1.26 | 0.209 | 0.209 | −0.22 |
| **BMI** | 23.23±1.64 | 29.26±2.36 | 16.80 | $2.07\times10^{-32}$ | $1.65\times10^{-31}$ | 2.95 |
| **Waist circumference** | 82.76±6.91 | 98.95±6.08 | 14.07 | $1.84\times10^{-27}$ | $7.36\times10^{-27}$ | 2.47 |
| **Systolic BP** | 114.47±7.76 | 129.50±9.77 | 9.64 | $1.27\times10^{-16}$ | $2.03\times10^{-16}$ | 1.69 |
| **Diastolic BP** | 75.50±6.02 | 83.89±7.27 | 7.11 | $8.42\times10^{-11}$ | $1.19\times10^{-10}$ | 1.25 |
| **Triglycerides** | 122.05±28.91 | 210.33±51.77 | 11.91 | $8.23\times10^{-21}$ | $1.80\times10^{-20}$ | 2.09 |
| **HDL-C** | 48.58±4.84 | 38.52±5.81 | −10.65 | $4.03\times10^{-19}$ | $8.07\times10^{-19}$ | −1.87 |
| **LDL-C** | 114.32±23.34 | 137.58±22.58 | 5.73 | $6.95\times10^{-8}$ | $8.35\times10^{-8}$ | 1.01 |
| **Total cholesterol** | 188.02±25.81 | 218.17±29.21 | 6.19 | $8.16\times10^{-9}$ | $1.09\times10^{-8}$ | 1.09 |
| **Fasting glucose** | 91.92±6.19 | 146.76±24.20 | 17.56 | $1.36\times10^{-27}$ | $6.54\times10^{-27}$ | 3.09 |
| **Fasting insulin** | 8.24±2.27 | 23.94±6.10 | 19.29 | $7.27\times10^{-32}$ | $4.36\times10^{-31}$ | 3.39 |
| **HOMA-IR** | 1.87±0.54 | 8.85±3.10 | 17.72 | $5.87\times10^{-27}$ | $1.76\times10^{-26}$ | 3.11 |
| **HbA1c** | 5.26±0.24 | 6.77±0.69 | 16.50 | $4.18\times10^{-27}$ | $1.43\times10^{-26}$ | 2.90 |
| **MDA** | 3.89±0.52 | 4.71±0.52 | 8.90 | $5.05\times10^{-15}$ | $7.57\times10^{-15}$ | 1.56 |
| **TBARS** | 5.95±0.67 | 8.89±0.61 | 25.95 | $4.13\times10^{-52}$ | $4.96\times10^{-51}$ | 4.56 |
| **SOD** | 14.16±0.51 | 13.46±0.78 | −6.01 | $2.54\times10^{-8}$ | $3.21\times10^{-8}$ | −1.06 |
| **Catalase** | 178.93±14.05 | 174.40±19.26 | −1.52 | 0.131 | 0.137 | −0.27 |
| **GPx** | 296.04±77.79 | 246.61±82.57 | −3.49 | $6.77\times10^{-4}$ | $7.38\times10^{-4}$ | −0.61 |
| **GSH** | 8.54±1.65 | 6.90±2.02 | −5.04 | $1.66\times10^{-6}$ | $1.90\times10^{-6}$ | −0.89 |
| **IL-6** | 1.66±0.55 | 3.56±0.98 | 13.57 | $2.51\times10^{-24}$ | $6.70\times10^{-24}$ | 2.38 |
| **TNF-α** | 2.85±0.67 | 4.80±1.00 | 12.93 | $7.87\times10^{-24}$ | $1.89\times10^{-23}$ | 2.27 |
| **CRP** | 1.37±0.68 | 3.24±1.30 | 10.12 | $9.15\times10^{-17}$ | $1.57\times10^{-16}$ | 1.78 |
| **ESR** | 6.73±3.04 | 15.13±5.80 | 10.27 | $4.37\times10^{-17}$ | $8.06\times10^{-17}$ | 1.80 |
| **MetS component count** | 0.58±0.69 | 4.22±0.83 | 27.14 | $1.67\times10^{-53}$ | $4.01\times10^{-52}$ | 4.77 |

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After FDR correction, 22 of 24 outcomes were statistically significant. Age and catalase were not significant. The largest standardized case-control differences were found for:

- Metabolic-syndrome component count: Hedges' g=4.77.
- TBARS: g=4.56.
- Fasting insulin: g=3.39.
- HOMA-IR: g=3.11.
- Fasting glucose: g=3.09.
- BMI: g=2.95.
- HbA1c: g=2.90.
- Waist circumference: g=2.47.

**Table 2.** Five-group Welch ANOVA results

| Variable | Welch F ($df_1$, $df_2$) | Raw p | FDR q | $Eta^2$ |
|---|---|---|---|---|
| **Age** | 0.63 (4, 28.9) | 0.644 | 0.644 | 0.020 |
| **BMI** | 68.32 (4, 28.1) | $4.72\times10^{-14}$ | $1.63\times10^{-13}$ | 0.704 |
| **Waist circumference** | 51.05 (4, 30.5) | $4.43\times10^{-13}$ | $1.33\times10^{-12}$ | 0.616 |
| **Systolic BP** | 31.83 (4, 29.9) | $2.17\times10^{-10}$ | $4.34\times10^{-10}$ | 0.482 |
| **Diastolic BP** | 30.72 (4, 30.8) | $2.35\times10^{-10}$ | $4.34\times10^{-10}$ | 0.461 |
| **Triglycerides** | 50.11 (4, 27.8) | $2.52\times10^{-12}$ | $6.73\times10^{-12}$ | 0.659 |
| **HDL-C** | 28.32 (4, 29.5) | $9.95\times10^{-10}$ | $1.71\times10^{-9}$ | 0.497 |
| **LDL-C** | 11.13 (4, 31.4) | $9.74\times10^{-6}$ | $1.17\times10^{-5}$ | 0.258 |
| **Total cholesterol** | 15.15 (4, 30.2) | $6.71\times10^{-7}$ | $8.95\times10^{-7}$ | 0.329 |
| **Fasting glucose** | 101.74 (4, 25.1) | $3.81\times10^{-15}$ | $1.83\times10^{-14}$ | 0.773 |
| **Fasting insulin** | 136.73 (4, 27.5) | $9.60\times10^{-18}$ | $7.68\times10^{-17}$ | 0.819 |
| **HOMA-IR** | 111.60 (4, 25.0) | $1.42\times10^{-15}$ | $8.51\times10^{-15}$ | 0.808 |
| **HbA1c** | 79.42 (4, 25.6) | $4.76\times10^{-14}$ | $1.63\times10^{-13}$ | 0.734 |
| **MDA** | 22.58 (4, 30.7) | $9.06\times10^{-9}$ | $1.36\times10^{-8}$ | 0.412 |
| **TBARS** | 186.62 (4, 31.5) | $1.83\times10^{-21}$ | $4.40\times10^{-20}$ | 0.845 |
| **SOD** | 12.44 (4, 27.7) | $6.51\times10^{-6}$ | $8.22\times10^{-6}$ | 0.285 |
| **Catalase** | 1.21 (4, 28.7) | 0.328 | 0.343 | 0.045 |
| **GPx** | 3.73 (4, 28.9) | 0.014 | 0.016 | 0.102 |
| **GSH** | 7.25 (4, 29.0) | $3.56\times10^{-4}$ | $4.07\times10^{-4}$ | 0.202 |
| **IL-6** | 46.03 (4, 27.4) | $8.73\times10^{-12}$ | $1.90\times10^{-11}$ | 0.618 |
| **TNF-α** | 44.93 (4, 28.3) | $7.30\times10^{-12}$ | $1.75\times10^{-11}$ | 0.612 |
| **CRP** | 24.94 (4, 27.1) | $9.73\times10^{-9}$ | $1.37\times10^{-8}$ | 0.450 |
| **ESR** | 26.06 (4, 27.2) | $5.76\times10^{-9}$ | $9.22\times10^{-9}$ | 0.471 |
| **MetS component count** | 170.13 (4, 28.7) | $1.51\times10^{-19}$ | $1.81\times10^{-18}$ | 0.856 |

The five-group ANOVA also showed significant phenotype differences for 22 of 24 outcomes after FDR correction. Age and catalase remained non-significant.
The strongest phenotype effects according to eta-squared were:

- MetS component count: $\eta^2$=0.856.
- TBARS: $\eta^2$=0.845.
- Fasting insulin: $\eta^2$=0.819.
- HOMA-IR: $\eta^2$=0.808.
- Fasting glucose: $\eta^2$=0.773.
- HbA1c: $\eta^2$=0.734.
- BMI: $\eta^2$=0.704.
- Triglycerides: $\eta^2$=0.659.

## Discussion

The presence of several metabolic disorders, including insulin resistance, dyslipidemia, oxidative stress, and chronic low-grade inflammation, is what defines metabolic syndrome. A total of 128 participants—64 with metabolic syndrome and 64 healthy controls—were assessed in this study. Anthropometric, glycemic, lipid, oxidative stress, antioxidant, and inflammatory indicators all showed distinct differences between the two groups. All things considered, the findings lend credence to the idea that metabolic syndrome is linked to a widespread change in metabolic and biochemical homeostasis rather than a singular anomaly in a particular biomarker.
Significant differences between the patients and controls were shown by the anthropometric and cardiometabolic results. BMI, waist circumference, systolic and diastolic blood pressure,

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triglycerides, LDL and total cholesterol, and HDL cholesterol were all greater in participants with metabolic syndrome. These results are in line with the clinical traits typically linked to metabolic syndrome and are similar to findings documented in earlier research [22]. The case group showed clustering of multiple cardiometabolic abnormalities rather than a single metabolic disturbance, as seen by the significant difference in metabolic-syndrome component count in the current investigation. The simultaneous existence of these problems may indicate the underlying interplay between altered lipid metabolism, poor insulin signaling, and enhanced oxidative and inflammatory processes, which makes this clustering significant.

The case group's altered insulin sensitivity and glucose metabolism were a particularly notable discovery. HbA1c, HOMA-IR, fasting insulin, and fasting plasma glucose were significantly greater in cases than in controls. Disturbances in glucose regulation and insulin sensitivity were among the most noticeable differences between the research groups, as seen by the substantial standardized differences found for fasting insulin, HOMA-IR, fasting glucose, and HbA1c. These results align with the established connection between metabolic syndrome and insulin resistance [23]. Increased HOMA-IR and elevated fasting insulin indicate that the affected individuals may have compensatory hyperinsulinemia in addition to decreased insulin sensitivity. Crucially, HOMA-IR also demonstrated positive correlations with a number of oxidative-stress and inflammatory markers in the current dataset, indicating that insulin resistance may arise within a more extensive biochemical milieu marked by oxidative imbalance and inflammation.

Additional proof of metabolic disruption in the case group is provided by the oxidative-stress findings. Participants with metabolic syndrome had significantly higher levels of MDA and TBARS, with TBARS exhibiting one of the biggest standardized case-control differences. An imbalance between the generation of reactive oxygen species and antioxidant defense mechanisms may be the cause of increased lipid peroxidation, which is a sign of increased oxidative damage. Previous studies have linked mitochondrial dysfunction to metabolic and obesity-related problems and have similarly defined oxidative stress as a significant component of metabolic syndrome [7, 9, 16]. Thus, the significant variation in TBARS found in this study is in line with the hypothesis that oxidative damage plays a role in metabolic inefficiency.

An opposite pattern was displayed by the antioxidant biomarkers. While catalase showed significant overlap between cases and controls and was not statistically significant, SOD, GPx, and GSH tended to be lower in the case group. Although the response is not consistent across all antioxidant systems, this pattern implies that antioxidant defenses may be changed in metabolic syndrome. Because it shows that not every portion of the antioxidant defense system reacts to the metabolic phenotype in the same way, the lack of substantial variation in catalase is especially important. Similar findings of antioxidant imbalance and oxidative stress have been documented in metabolic syndrome and associated metabolic illnesses [16, 24]. Therefore, evaluating multiple antioxidant indicators instead of just one may give a more accurate picture of the oxidative state of people with metabolic syndrome.

Additionally, there were significant differences in inflammatory biomarkers between the study groups. Participants with metabolic syndrome had higher levels of IL-6, TNF-α, CRP, and ESR; IL-6 and TNF-α showed especially substantial differences between cases and controls. These results corroborate the idea that the metabolic anomalies seen in the case group are accompanied by an inflammatory component. Inflammation, adiponectin, oxidative stress, and metabolic syndrome have all been linked in earlier investigations [20], and more recent clinical research has shown links between inflammatory markers and cardiometabolic illness [25]. Therefore, the idea that these processes may work as interrelated components of metabolic dysfunction is consistent with the simultaneous rise of oxidative-stress and inflammatory indicators in the current investigation.

The correlation matrix demonstrates clustering of metabolic, glycemic, oxidative-stress, and inflammatory measurements, which were predominantly positively correlated. HDL cholesterol and antioxidant-defense biomarkers generally showed inverse relationships with the adverse metabolic and inflammatory profile.

Additional proof of multivariate distinction between patients and controls came from the principal component analysis. The case group displayed higher dispersion than the control group, and the first main component accounted for 55.3% of the total variance. This distinction suggests that there were significant differences between the two phenotypes' combined biomarker profiles. Heterogeneity in the biochemical symptoms of metabolic syndrome may also be reflected in the wider dispersion among cases. Studies looking into metabolic syndrome and related metabolic diseases have shown similar indications of complicated metabolic and oxidative changes [26-29]. Crucially, by showing that

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the difference between cases and controls was visible over the entire biomarker profile rather than being influenced by a single variable, the multivariate results supplement the individual biomarker analyses.

Another significant finding of the current study is the correlation between HOMA-IR and oxidative-stress and inflammatory biomarkers. Positive correlations were found between HOMA-IR and IL-6, TNF-α, CRP, ESR, MDA, and TBARS. This pattern implies that the study population had higher levels of oxidative stress and systemic inflammation together with higher levels of insulin resistance. Such a correlation is in line with the more general knowledge that inflammation and insulin resistance are closely related metabolic processes. The significance of insulin resistance in the metabolic phenotype has been supported by other studies that looked into the connection between insulin resistance and metabolic syndrome [23, 30, 31].

Overall, the current study shows that metabolic syndrome is linked to a wide range of biochemical changes, including inflammation, oxidative stress, insulin resistance, and antioxidant defense. A more thorough description of the metabolic phenotype could be obtained by combining traditional metabolic studies with oxidative and inflammatory indicators. These biomarker associations may be useful for early detection, risk assessment, and monitoring of metabolic dysfunction if they are further validated in broader clinical populations.

## Conclusion

This study concludes that, when compared to controls, metabolic syndrome can have a substantial impact on a number of biomarkers related to oxidative stress, inflammation, and insulin resistance. In order to reduce the elevated levels of oxidative stress and inflammation in metabolic syndrome instances, targeting therapy must be implemented.

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