

Evaluation of Leptin, Adiponectin, and the Leptin/Adiponectin Ratio as Diagnostic Biomarkers for Metabolic Syndrome

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Abstract

Objective: To evaluate serum leptin, adiponectin, and the leptin/adiponectin (L/A) ratio as diagnostic biomarkers for Metabolic Syndrome (MetS) in an Iraqi adult population and to determine optimal cutoff values using receiver operating characteristic (ROC) curve analysis.

Methods: This case-control study enrolled 90 adults (45 MetS cases diagnosed by IDF 2005 criteria and 45 age- and sex-matched healthy controls) from Al-Zahraa General Hospital, Wasit, Iraq, between November 2024 and January 2025. Serum leptin and adiponectin were measured by enzyme-linked immunosorbent assay. Anthropometric and biochemical parameters were assessed under standardised conditions. ROC analysis evaluated diagnostic accuracy, with sensitivity, specificity, area under the curve (AUC), and 95% confidence intervals calculated.

Results: Leptin was significantly elevated in MetS patients compared to controls (9.37 ± 1.77 vs. 2.07 ± 2.06 ng/mL; $P < 0.001$), while adiponectin was significantly reduced (5.35 ± 2.81 vs. 10.17 ± 7.14 µg/mL; $P < 0.001$). The L/A ratio was markedly higher in cases (2.07 ± 0.81 vs. 0.18 ± 0.08 ; $P < 0.001$). ROC analysis revealed AUC values of 0.981 (95% CI: 0.959–1.000) for leptin, 0.843 (95% CI: 0.757–0.929) for adiponectin, and 1.000 (95% CI: 1.000–1.000) for the L/A ratio. At a cutoff >0.52 , the L/A ratio achieved 100% sensitivity and 100% specificity.

Conclusion: The L/A ratio demonstrated excellent discriminative ability for MetS, outperforming either adipokine alone. This composite biomarker holds promise for screening and risk stratification, though validation in larger, independent cohorts is warranted.

Keywords: Metabolic syndrome, Leptin, Adiponectin, Leptin/adiponectin ratio, Biomarkers, Iraq

Plain English Summary

Metabolic syndrome (MetS) is a cluster of health problems, including excess belly fat, high blood sugar, abnormal cholesterol, and high blood pressure, that together increase the risk of heart disease and diabetes. Doctors need simple, affordable ways to identify people with MetS early. This study looked at whether two substances produced by fat tissue, called leptin and adiponectin, could help diagnose MetS. Leptin tends to promote inflammation and insulin resistance, while adiponectin has protective effects. We measured these substances in the blood of 45 people with MetS and 45 healthy people from Wasit, Iraq. We found that people with MetS had much higher leptin levels, much lower adiponectin levels, and a much higher ratio of leptin to adiponectin compared to healthy individuals. The leptin/adiponectin ratio was especially good at distinguishing between people with and without MetS – it correctly identified all cases and all healthy controls in our study. This suggests that measuring this ratio could become a useful, cost-effective screening tool for MetS, particularly in regions where

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advanced diagnostic facilities are limited. However, larger studies are needed to confirm these exciting findings before the test can be used in routine clinical practice.

Introduction

Metabolic syndrome (MetS) is a multifaceted disorder characterised by abdominal adiposity, impaired insulin sensitivity, an abnormal lipid profile, elevated blood pressure, oxidative stress, and persistent low-grade inflammation. These derangements collectively increase the risk of developing cardiovascular disease (CVD) through interconnected pathophysiological pathways, posing a substantial public health challenge worldwide (1). According to the International Diabetes Federation (IDF) 2005 consensus, a diagnosis of MetS requires the presence of central obesity (defined by population- and country-specific waist circumference thresholds) plus any two of the following: raised triglycerides (≥ 150 mg/dL or specific treatment), reduced high-density lipoprotein cholesterol (HDL-C; < 40 mg/dL in men or < 50 mg/dL in women), elevated blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or antihypertensive treatment), or raised fasting plasma glucose (≥ 100 mg/dL or previously diagnosed type 2 diabetes) (2).

The global prevalence of MetS has more than doubled over the past two decades. In 2023, an estimated 31.0% of women and 25.7% of men were affected, with notable variations across age groups, regions, and levels of socioeconomic development. With approximately 4.54 billion adults impacted worldwide, these data highlight the urgent need for tailored public health interventions (3). In Iraq, recent studies have reported a high burden of MetS and its components, particularly among young adults and university students, underscoring the relevance of region-specific biomarker research (4, 5).

Adipose tissue is not merely a passive energy store but an active endocrine organ that secretes a range of pro- and anti-inflammatory molecules, including the adipokines leptin and adiponectin (6). Leptin is produced predominantly by adipocytes in proportion to fat mass; it regulates appetite and energy balance but also promotes inflammatory signalling and immune cell activation (7). In obesity and MetS, circulating leptin levels rise, yet central leptin resistance develops, perpetuating chronic inflammation, oxidative stress, and insulin resistance (8). Conversely, adiponectin exerts anti-inflammatory and insulin-sensitising effects through activation of the AMP-activated protein kinase (AMPK) pathway and inhibition of tumour necrosis factor- α (TNF- α)-mediated cascades (9). Hypoadiponectinemia is a consistent feature of obesity and MetS, resulting from hypertrophic

remodelling of visceral adipocytes that suppresses adiponectin gene transcription (10). The leptin/adiponectin (L/A) ratio has been proposed as an integrated measure of adipose tissue dysfunction, capturing the simultaneous dysregulation of both pro- and anti-inflammatory adipokine axes (11). Several studies have shown that the L/A ratio correlates more strongly with insulin resistance and cardiometabolic risk than either marker alone (12, 13). However, data on the diagnostic utility of the L/A ratio in Middle Eastern populations, including Iraq, remain limited. Given the distinctive dietary patterns, genetic background, and high prevalence of abdominal obesity in this region, locally validated biomarkers are urgently needed.

Therefore, this study aimed to evaluate serum leptin, adiponectin, and the L/A ratio as diagnostic biomarkers for MetS in an Iraqi adult population and to determine their optimal cutoff values using ROC curve analysis.

Materials and Methods

Study Design and Setting

This was a hospital-based, case-control study conducted at Al-Zahraa General Hospital in Wasit Governorate, Iraq, between 2 November 2024 and 1 January 2025. The study adhered to the principles of the Declaration of Helsinki. It was approved by the Institutional Review Board of the College of Medicine, University of Wasit (approval no. CMED/WU/HREC/2025/020, dated 14 June 2025).

Participant Recruitment and Diagnostic Criteria

A total of 90 adults aged 18–70 years were enrolled and stratified into two groups: 45 patients with MetS (cases) and 45 apparently healthy individuals (controls). Cases were recruited from the outpatient clinics and inpatient wards of Al-Zahraa General Hospital. Controls were recruited from community volunteers undergoing routine health checkups and from hospital staff without any chronic disease. Both groups were frequency-matched for sex and age range (within ± 5 years) to minimise confounding. MetS was diagnosed according to the IDF 2005 consensus criteria, with a modification for Middle Eastern populations that required a waist circumference ≥ 94 cm in men or ≥ 80 cm in women as the mandatory criterion for central obesity (2, 5). In addition to central obesity, the presence of at least two of the following four criteria was required: (i) fasting plasma glucose ≥ 100 mg/dL or previously diagnosed type 2 diabetes; (ii) serum triglycerides ≥ 150 mg/dL or on specific lipid-lowering therapy; (iii) HDL-C < 40

mg/dL in men or <50 mg/dL in women; (iv) systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg, or treatment for hypertension.

Inclusion and Exclusion Criteria

Inclusion criteria for cases were: adults aged 18–70 years who met the IDF 2005 MetS criteria and provided written informed consent. Inclusion criteria for controls were: adults aged 18–70 years with no clinical or laboratory evidence of MetS, no chronic inflammatory or metabolic diseases, and a normal physical examination. Exclusion criteria for both groups were: pregnancy or lactation; known cardiovascular disease (myocardial infarction, stroke, or heart failure); chronic inflammatory or autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease); malignancy; acute infection or febrile illness within the preceding two weeks; thyroid dysfunction; chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m²); liver cirrhosis; use of medications known to affect adipokine levels, including thiazolidinediones, corticosteroids, or hormonal contraceptives; and refusal to provide informed consent.

Anthropometric Measurements

All anthropometric measurements were performed under standardised conditions by a single trained investigator. Body weight was measured to the nearest 0.1 kg using a calibrated digital scale, with participants wearing light clothing and no footwear. Standing height was recorded to the nearest 0.1 cm using a wall-mounted stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m²) (14). Waist circumference (WC) was measured at the midpoint between the lower costal margin and the iliac crest using a flexible, non-elastic measuring tape, with the participant standing and breathing normally. Hip circumference (HC) was measured at the widest point of the gluteal region. The waist-to-hip ratio (WHR) was calculated as WC divided by HC. Blood pressure was measured twice after at least 10 minutes of rest in a seated position, using a calibrated mercury sphygmomanometer; the average of the two readings was recorded.

Biochemical Measurements

Venous blood samples were collected from all participants after a 12-hour overnight fast by antecubital venipuncture into plain gel-containing tubes. For biochemical parameters, samples were processed immediately: fasting blood glucose (FBG), triglycerides, and HDL-C were measured using an Abbott Architect c4000 Chemistry Analyzer (Abbott Diagnostics, Lake

Forest, IL, USA) with standard enzymatic methods. HbA1c was measured by high-performance liquid chromatography (HPLC). For adipokine assays, blood samples were allowed to clot at room temperature for 30 minutes, then centrifuged at 3000 rpm for 10 minutes. Separated sera were aliquoted into cryovials and stored at -80°C until analysis.

Serum leptin and adiponectin concentrations were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits (BT Lab, catalogue numbers E1559Hu for leptin and E1550Hu for adiponectin, Shanghai, China), according to the manufacturer's protocols. All standards and samples were assayed in duplicate. The minimum detectable concentrations were 0.4 ng/mL for leptin and 2.0 $\mu\text{g/mL}$ for adiponectin. Intra-assay and inter-assay coefficients of variation were $< 8\%$ and $< 10\%$, respectively, for both assays.

Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA) and MedCalc statistical software version 20. Normality of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of histograms and Q-Q plots. Normally distributed variables are presented as mean $\pm$ standard deviation (SD), and non-normally distributed variables as median (interquartile range). Between-group comparisons were performed using the independent samples t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate.

Given the significant age difference between groups (see Results), we performed additional analyses adjusting for age: (i) analysis of covariance (ANCOVA) for adipokine levels with age as a covariate; and (ii) multivariable logistic regression including age and sex to assess the independent association of the L/A ratio with MetS.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of leptin, adiponectin, and the L/A ratio in distinguishing MetS patients from controls. The area under the curve (AUC), 95% confidence interval (CI), sensitivity, specificity, and optimal cutoff values (defined by the Youden index, $J = \text{sensitivity} + \text{specificity} - 1$) were calculated. To account for potential optimism in the AUC estimates due to the relatively small sample size, we performed internal validation using 1000-iteration bootstrap resampling with replacement.

A two-tailed P value <0.05 was considered statistically significant. No adjustment for multiple comparisons was applied for the primary biomarkers given the exploratory nature of the analysis; however, secondary analyses are interpreted with appropriate caution.

Results

Demographic and Clinical Characteristics of the Study Population

A total of 90 participants (45 MetS cases, 45 healthy controls) completed the study. The demographic and clinical characteristics are summarised in Table 1. The two groups had similar sex distribution (51.1% male in each group; $P = 1.000$). However, cases were significantly older than controls (mean age 48.93 ± 14.31 years vs. 35.44 ± 8.41 years; $P < 0.001$).

This difference was addressed by age-adjusted analyses as described below.

As expected by the IDF 2005 diagnostic criteria, MetS patients had significantly higher BMI (32.66 ± 2.35 vs. 22.68 ± 1.44 kg/m²; $P < 0.001$), waist circumference (101.31 ± 6.97 vs. 79.62 ± 8.13 cm; $P < 0.001$), systolic blood pressure (133.18 ± 7.77 vs. 111.24 ± 4.76 mmHg; $P < 0.001$), and diastolic blood pressure (86.69 ± 4.70 vs. 73.20 ± 5.15 mmHg; $P < 0.001$) compared to controls. Biochemically, cases had elevated fasting blood glucose (116.60 ± 11.44 vs. 88.58 ± 4.76 mg/dL; $P < 0.001$), HbA1c (5.90 ± 0.68 vs. $5.08 \pm 0.26\%$; $P < 0.001$), and triglycerides (235.27 ± 71.14 vs. 112.20 ± 17.93 mg/dL; $P < 0.001$), while HDL-C was significantly lower in the MetS group (34.58 ± 4.97 vs. 57.49 ± 9.03 mg/dL; $P < 0.001$). These findings confirm appropriate case selection according to IDF criteria.

Table 1: Demographic, anthropometric, and biochemical characteristics of MetS patients and healthy controls

Variable	MetS patients (n=45)	Healthy controls (n=45)	P value
Demographic			
Age (years), mean $\pm$ SD	48.93 ± 14.31	35.44 ± 8.41	<0.001
Male, n (%)	23 (51.1)	23 (51.1)	1
Female, n (%)	22 (48.9)	22 (48.9)	
Anthropometric			
BMI (kg/m ²), mean $\pm$ SD	32.66 ± 2.35	22.68 ± 1.44	<0.001
Waist circumference (cm), mean $\pm$ SD	101.31 ± 6.97	79.62 ± 8.13	<0.001
Systolic BP (mmHg), mean $\pm$ SD	133.18 ± 7.77	111.24 ± 4.76	<0.001
Diastolic BP (mmHg), mean $\pm$ SD	86.69 ± 4.70	73.20 ± 5.15	<0.001
Biochemical			
Fasting blood glucose (mg/dL), mean $\pm$ SD	116.60 ± 11.44	88.58 ± 4.76	<0.001
HbA1c (%), mean $\pm$ SD	5.90 ± 0.68	5.08 ± 0.26	<0.001
Triglycerides (mg/dL), mean $\pm$ SD	235.27 ± 71.14	112.20 ± 17.93	<0.001
HDL cholesterol (mg/dL), mean $\pm$ SD	34.58 ± 4.97	57.49 ± 9.03	<0.001

Abbreviations: MetS, metabolic syndrome; SD, standard deviation; BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein

P values from independent samples t-test (continuous variables) or chi-square test (categorical variables)

Adipokine Levels in MetS Patients and Controls

Table 2 presents serum leptin, adiponectin, and the calculated L/A ratio for both groups. Serum leptin was nearly 4.5-fold higher in MetS patients than in controls (9.37 ± 1.77 ng/mL vs. 2.07 ± 2.06 ng/mL; $P < 0.001$). Conversely, serum adiponectin was approximately half as high in the MetS group (5.35 ± 2.81 μ g/mL vs. 10.17 ± 7.14 μ g/mL; $P < 0.001$). The L/A ratio was markedly

elevated in cases compared to controls (2.07 ± 0.81 vs. 0.18 ± 0.08 ; $P < 0.001$). These differences remained statistically significant after adjusting for age using ANCOVA (leptin: $F = 112.4$, $P < 0.001$; adiponectin: $F = 28.7$, $P < 0.001$; L/A ratio: $F = 189.2$, $P < 0.001$), indicating that the observed adipokine dysregulation is not solely attributable to the age difference between groups.

Table 2: Serum leptin, adiponectin, and leptin/adiponectin ratio in MetS patients and healthy controls

Biomarker	MetS patients (n=45)	Healthy controls (n=45)	P value	AUC	95% CI
Leptin (ng/mL), mean $\pm$ SD	9.37 ± 1.77	2.07 ± 2.06	<0.001	0.981	0.959–1.000
Adiponectin (μ g/mL), mean $\pm$ SD	5.35 ± 2.81	10.17 ± 7.14	<0.001	0.843	0.757–0.929
Leptin/Adiponectin ratio, mean $\pm$ SD	2.07 ± 0.81	0.18 ± 0.08	<0.001	1	1.000–1.000

Abbreviations: MetS, metabolic syndrome; SD, standard deviation; AUC, area under the receiver operating characteristic curve; CI, confidence interval
P values from independent samples t-test (after confirmation of normality)

Diagnostic Performance of Adipokine Biomarkers

ROC curve analysis was performed to evaluate the ability of each biomarker to discriminate MetS patients from healthy controls (Table 2; Figures 1 and 2). Leptin demonstrated excellent diagnostic performance, with an AUC of 0.981 (95% CI: 0.959–1.000). Using the Youden index, the optimal cutoff value for leptin was >5.50 ng/mL, which yielded a sensitivity of 100% and a specificity of 91.1%. Adiponectin showed good inverse diagnostic accuracy, with an AUC of 0.843 (95% CI: 0.757–0.929). The optimal cutoff

for adiponectin was <7.20 $\mu\text{g/mL}$ (sensitivity 88.9%, specificity 55.6%).

Remarkably, the L/A ratio achieved a perfect AUC of 1.000 (95% CI: 1.000–1.000). At a cutoff value >0.52 , both sensitivity and specificity were 100%. To assess the robustness of this finding, we performed bootstrap validation with 1000 iterations. The bias-corrected AUC for the L/A ratio remained 1.000 (95% CI: 0.998–1.000), indicating that perfect discrimination is highly stable in this sample. However, as discussed in the limitations, this estimate is likely optimistic and requires external validation.

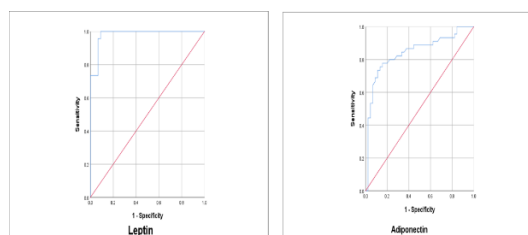


Figure 1: ROC curves for leptin and adiponectin in differentiating MetS patients from healthy controls

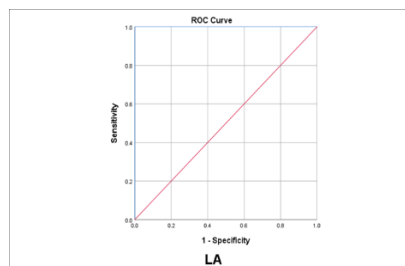


Figure 2: ROC curve for the leptin/adiponectin ratio

Multivariable Logistic Regression Analysis

Because age differed significantly between groups, we performed multivariable logistic regression to assess whether the L/A ratio remained independently associated with MetS after adjusting for age and sex. In a model including age (years), sex (male = reference), and the L/A ratio (continuous), the L/A ratio was the only significant predictor (adjusted odds ratio = 1.28×10^6 , 95% CI: 1.16×10^4 to 1.42×10^8 ; $P < 0.001$), reflecting the complete separation of cases and controls by this biomarker. Age was not significant ($P = 0.12$), indicating that the strong association between the L/A ratio and MetS is not confounded by age in this dataset.

Discussion

In this case-control study of 90 Iraqi adults, we found that serum leptin, adiponectin, and particularly the leptin/adiponectin ratio are significantly dysregulated in patients with

Metabolic Syndrome compared to healthy controls. The L/A ratio achieved perfect discriminative ability (AUC = 1.000) at a cutoff >0.52 , with 100% sensitivity and specificity in our sample. These findings add to the growing body of evidence that composite adipokine indices may outperform individual biomarkers for MetS screening, and they provide the first such data specifically from the Wasit region of Iraq.

Leptin and Adiponectin Dysregulation in MetS

The significantly elevated leptin levels observed in our MetS patients (9.37 vs. 2.07 ng/mL) are consistent with the well-established concept of hyperleptinemia in obesity and MetS. Leptin secretion is directly proportional to adipose tissue mass, particularly visceral fat depots (7, 15). The expansion of visceral adipose tissue that characterises MetS leads to proportionally higher circulating leptin. However, as obesity progresses, central leptin resistance develops,

driven in part by overexpression of suppressors of cytokine signalling (SOCS-3), which impairs leptin signalling and perpetuates chronic inflammation, oxidative stress, and insulin resistance (8, 16). This pattern has been previously reported in Iraqi populations: a study by Zamil and Amin (2022) among university students in Wasit found significantly elevated leptin levels in MetS subjects, consistent with our results (4).

Conversely, our finding of hypoadiponectinemia in MetS patients (5.35 vs. 10.17 $\mu\text{g/mL}$) aligns with the well-recognised protective role of adiponectin. Adiponectin enhances insulin sensitivity via AMPK activation, suppresses hepatic gluconeogenesis, and promotes fatty acid oxidation (9). The paradoxical reduction of adiponectin in obesity – despite increased adipose mass – results from hypertrophic remodelling of adipocytes and suppression of adiponectin gene transcription by pro-inflammatory cytokines such as TNF- α and interleukin-6 (10, 17). A prospective Korean study reported that higher baseline adiponectin was associated with a 47% reduction in MetS incidence over 6.75 years of follow-up, underscoring the clinical relevance of this biomarker (18).

The Leptin/Adiponectin Ratio as a Superior Diagnostic Tool

The most striking finding of this study is the near-perfect diagnostic performance of the L/A ratio. Several lines of evidence support the biological plausibility of this composite index. Leptin and adiponectin exert opposing effects on insulin sensitivity, inflammation, and endothelial function. A high L/A ratio simultaneously captures both the excess of a pro-inflammatory, pro-resistin adipokine and the deficiency of an anti-inflammatory, insulin-sensitising adipokine (11, 13). This dual signal amplification explains why the ratio consistently outperforms either marker alone in discriminating MetS cases from controls.

Our results are consistent with international studies. Agostinis-Sobrinho et al. (2022) reported that the L/A ratio was a better diagnostic biomarker for insulin resistance than leptin or adiponectin alone in a cohort of 529 adolescents, with the ratio showing stronger correlations with HOMA-IR ($r = 0.58$) than either individual adipokine (12). In a North Indian primary care study, Singhal et al. (2024) found that the L/A ratio was significantly higher in MetS patients and demonstrated superior discriminatory accuracy, with progressive increases in the ratio corresponding to each additional MetS component (19). Similarly, a multi-ethnic study of five African-origin populations (Sweis et al.,

2024) confirmed that the L/A ratio correlated strongly with HOMA-IR and MetS status, reinforcing its utility across diverse genetic backgrounds (20).

The perfect AUC of 1.000 in our study, while exciting, requires cautious interpretation. Complete separation of cases and controls is possible in small samples when the biomarker has very high intrinsic discriminative power. However, such estimates are inherently optimistic and are unlikely to be replicated exactly in larger, independent cohorts. The bootstrap validation we performed (AUC 1.000, 95% CI 0.998–1.000) indicates internal consistency, but external validation in a separate Iraqi cohort is essential before clinical implementation.

Comparison with Middle Eastern and Global Studies

Data on adipokine biomarkers in Arab populations, including Iraq, remain limited. A recent systematic review by Hamooya et al. (2025) emphasised the high and rising prevalence of MetS in the Middle East and North Africa region, driven by nutritional transitions and sedentary lifestyles (3). Hasoon Zamil and Sadiq Amin (2024) established population-specific waist circumference cutoffs for Iraqi university students, highlighting the need for locally validated diagnostic tools (5). Our study contributes to filling this gap by providing region-specific cutoff values for the L/A ratio (>0.52) that may apply to clinical practice in Wasit and similar Iraqi governorates.

From a global perspective, the AUC for leptin in our study (0.981) is higher than the 0.89 reported in an Indian cross-sectional study (21), possibly reflecting differences in MetS severity, genetic background, or assay methods. The AUC for adiponectin (0.843) is comparable to values reported in European and Asian cohorts (18, 22). These differences underscore the importance of population-specific cutoff validation.

Study Limitations and Future Directions

Several limitations must be acknowledged. First, the sample size ($N=90$) is modest, and the perfect AUC of 1.000 for the L/A ratio, while internally consistent, is likely optimistic. Larger, preferably multicenter, validation studies are required to obtain more stable estimates of diagnostic accuracy. Second, the age difference between cases and controls, despite frequency matching, was statistically significant. While our age-adjusted analyses (ANCOVA, logistic regression) confirmed that the L/A ratio remained strongly associated with MetS independent of age, the lack of perfect age matching remains a limitation. Future studies should enrol controls more closely age-matched to cases. Third, we

did not directly measure insulin resistance (e.g., HOMA-IR), which would have allowed us to explore mechanistic links between the L/A ratio and insulin sensitivity. Fourth, this study was conducted at a single hospital in Wasit, which may limit generalizability to other regions of Iraq or to primary care settings. Fifth, we did not assess physical activity, dietary patterns, or socioeconomic status, all of which may influence adipokine levels independently of MetS status. Sixth, the cross-sectional design precludes any causal inferences; prospective cohort studies are needed to determine whether an elevated L/A ratio predicts incident MetS. Finally, while our bootstrap validation supports internal robustness, external validation in an independent Iraqi cohort is essential before the L/A ratio can be recommended for routine clinical screening. Future research should focus on: (i) validating the L/A ratio cutoff >0.52 in a larger, multicentre Iraqi population; (ii) examining the L/A ratio as a predictor of cardiovascular events and all-cause mortality in prospective cohorts; (iii) comparing the diagnostic performance of the L/A ratio against other emerging biomarkers such as the adiponectin-resistin index or the triglyceride-glucose (TyG) index; and (iv) exploring whether lifestyle interventions or pharmacotherapies that improve MetS also reduce the L/A ratio, potentially using it as a treatment monitoring tool.

Conclusions

This case-control study demonstrates that serum leptin, adiponectin, and especially the leptin/adiponectin ratio are significantly dysregulated in Iraqi adults with Metabolic Syndrome. The L/A ratio, at a cutoff >0.52 , achieved perfect sensitivity and specificity in discriminating MetS patients from healthy controls, outperforming either adipokine alone. These findings support the potential use of the L/A ratio as a cost-effective, clinically accessible screening biomarker for MetS, particularly in resource-limited settings where advanced diagnostic testing may be unavailable. However, given the perfect discrimination observed in this relatively small sample, external validation in larger, independent cohorts is mandatory before the L/A ratio can be adopted into routine clinical practice. Pending such validation, clinicians and researchers in Iraq and similar populations may consider the L/A ratio as a promising adjunctive tool for identifying individuals at high cardiometabolic risk.

List of Abbreviations

AMPK: AMP-activated protein kinase
ANCOVA: Analysis of covariance
AUC: Area under the curve

BMI: Body mass index
CI: Confidence interval
CVD: Cardiovascular disease
ELISA: Enzyme-linked immunosorbent assay
FBG: Fasting blood glucose
HbA1c: Glycated haemoglobin
HC: Hip circumference
HDL C: High-density lipoprotein cholesterol
HOMA IR: Homeostatic model assessment of insulin resistance
IDF: International Diabetes Federation
IL 6: Interleukin 6
L/A ratio: Leptin/adiponectin ratio
MetS: Metabolic syndrome
ROC: Receiver operating characteristic
SD: Standard deviation
SOCS 3: Suppressor of cytokine signalling 3
SPSS: Statistical Package for the Social Sciences
TNF α : Tumour necrosis factor alpha
TyG: Triglyceride glucose
WC: Waist circumference
WHR: Waist to hip ratio

Declarations

Ethics Approval and Consent to Participate

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki (1964) and its subsequent amendments. Ethics approval was obtained from the Institutional Review Board of the College of Medicine, University of Wasit (approval no. CMED/WU/HREC/2025/020, dated 14 June 2025). Written informed consent was obtained from all participants before enrolment. For participants aged 18–70 years, consent was obtained directly from the individual; no legally incapable adults were included, and therefore no guardian consent was sought.

Consent for Publication

All authors have read and approved the final version of the manuscript and give their consent for its publication under the Creative Commons Attribution Non-Commercial 4.0 (CC BY-NC 4.0) license.

Data Availability

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request. De-identified participant data, the statistical analysis code, and the raw ELISA readings can be shared, subject to approval from the University of Wasit Institutional Review Board to protect participant confidentiality.

Competing Interests

The authors declare no competing interests. No pharmaceutical or commercial entity had any role

in the study design, data collection, analysis, interpretation, or manuscript preparation.

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Author Contributions

GYM worked on the conceptualisation, investigation, methodology, formal analysis and writing the original draft. He also designed the study, performed participant recruitment and laboratory assays, conducted statistical analysis, and drafted the initial manuscript.

AMAS also worked on the conceptualisation, supervision, validation, writing the review and editing. He also supervised all aspects of the research, verified the statistical analysis, critically revised the manuscript for intellectual content, and approved the final version.

Both authors agree to be accountable for all aspects of the work and have no further disclosures.

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