RESEARCH ARTICLE

ANGPTL4 and Caveolin-1 as potential novel biomarkers for metabolic syndrome in Iraqi adults over 50

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Background: Background: Metabolic syndrome (MetS) is a cluster of risk factors, including abdominal obesity, dyslipidemia, hyperglycemia and hypertension that markedly elevate the incidence of cardiovascular diseases and type 2 diabetes.

Objective: This study aimed to evaluate the diagnostic value of serum angiopoietin-like protein 4 (ANGPTL4) and Caveolin-1 (Cav-1), as novel agents in diagnosing MetS in patients older than 50 years.

Methods: A case-control study (January–April 2025) included 60 cases with MetS and 30 matched-healthy participants of the same gender and age (>50 years) from hospitals in Diyala Governorate, Iraq. MetS was diagnosed by harmonized definition (≥3 features: elevated waist diameter, triglyceride ≥150 mg/dL, low HDL-C, BP ≥130/85 mmHg and fasting glucose ≥100 mg/dL).

Results: Serum ANGPTL4 (142.78 ± 22.53 vs. 69.29 ± 30.80 ng/mL, p-value <0.001) and Cav-1 (16.12 ± 2.87 vs. 8.51 ± 1.59 ng/mL, p-value <0.001) were significantly elevated in the MetS group. Receiver Operating Characteristic (ROC) analysis demonstrated exceptional diagnostic performance, with an Area Under the Curve (AUC) of 0.97 for ANGPTL4 and 0.99 for Cav-1. Binary logistic regression analysis identified both biomarkers as significant independent predictors of MetS.

Conclusion: Serum ANGPTL4 and Caveolin-1 levels exhibited outstanding diagnostic performance for MetS in Iraqi adults aged >50 years, reflecting underlying lipid dysregulation and endothelial dysfunction. These biomarkers showed significant potential for enhancing early detection and clinical management, warranting validation in a broader population.

Keywords: metabolic syndrome, ANGPTL4, Caveolin-1, Iraq.

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Introduction

Metabolic syndrome (MetS) comprises a group of cardiometabolic risk factors including abdominal obesity, dyslipidemia, impaired glucose tolerance, and hypertension, which are thought to be associated with insulin resistance [1,2]. The increasing number of obese people and sedentary lifestyles are major contributing factors to the incidence of MetS, which is widespread and increasing globally. Type 2 diabetes mellitus (T2DM) is intimately linked to MetS and is associated with an increased risk of cardiovascular events [3].

MetS was defined according to the harmonized global consensus criteria [1], established collaboratively by international organizations including the International Diabetes Federation, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, and International Association for the Study of Obesity. Diagnosis required the presence of three or more of the following components: elevated waist circumference (≥94 cm in males, ≥80 cm in females); systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg; elevated fasting serum glucose (≥100 mg/dL); reduced high-density lipoprotein cholesterol (HDL-C) (<40 mg/dL in males, <50 mg/dL in females); and hypertriglyceridemia (serum triglycerides ≥150 mg/dL)[4,5]. The global prevalence of MetS is rising, affecting approximately 20–25% of adults worldwide, making it a significant public health concern [6,7]. While the harmonized diagnostic criteria are clinically useful, they primarily identify established metabolic dysfunction and may not fully capture the underlying pathophysiological heterogeneity or early stages of the disease [8]. This highlights a critical need for novel biomarkers that can enhance early detection, risk stratification, and provide deeper insights into the molecular mechanisms of MetS.

Among promising candidates, Angiopoietin-Like Protein 4 (ANGPTL4) and Caveolin-1 have emerged as key proteins implicated in the pathophysiology of MetS. ANGPTL4 is a secreted glycoprotein that plays a pivotal role in lipid metabolism by acting as a potent inhibitor of lipoprotein lipase (LPL), the primary enzyme responsible for clearing circulating triglycerides. By inhibiting LPL, elevated ANGPTL4 levels contribute directly to the hypertriglyceridemia characteristic of MetS [9,10]. Furthermore, ANGPTL4 is involved in inflammation and insulin resistance, linking it to multiple facets of the syndrome [11,12]. Caveolin-1 is an integral membrane protein essential for the formation of caveolae, which are specialized lipid raft domains involved in cellular signaling and trans-

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port. Cav-1 is a critical regulator of cholesterol homeostasis, insulin receptor signaling, and endothelial function. Dysregulation of Cav-1 has been associated with endothelial dysfunction, inflammation, and insulin resistance, all of which are core components of MetS [13,14]. Given the integral roles of these proteins in metabolic pathways, their quantification in circulation could offer a more direct and mechanistic assessment of MetS status than conventional clinical measures alone. The present study was to explore the diagnostic value of serum ANGPTL4 and Caveolin-1 compared with conventional metabolic indexes for MetS in adults aged > 50 years.

Materials and methods

This case-control study was conducted across multiple hospitals in the Diyala Governorate, Iraq between January and April 2025. The study population comprised 60 patients diagnosed with MetS and 30 age-matched healthy controls, all aged >50 years old. Sixty adults (>50 years old) with confirmed MetS (both sexes) were enrolled in this study. MetS diagnosis followed the standard criteria, requiring ≥3 of the following: abdominal obesity (waist circumference ≥94 cm [men]/≥80 cm [women]), hypertension (BP ≥130/85 mmHg or medication), fasting blood glucose ≥100 mg/dL or medication, hypertriglyceridemia (≥150 mg/dL), and low HDL cholesterol (<40 mg/dL [men]/<50 mg/dL [women]). Controls: Thirty healthy adults (aged >50 years, of both sexes) without MetS or other exclusionary conditions were recruited. The controls were matched for age and sex.

Inclusion and exclusion criteria

Participants were included in the study if they were aged >50 years. Cases were required to have a confirmed diagnosis of MetS as determined by a supervising physician, according to the harmonized criteria. Controls were healthy individuals without MetS, matched for age and sex.

Exclusion Criteria

To minimize confounding variables, participants were excluded if they presented with any of the following conditions or were using specific medications known to influence metabolic or bone health: Age: ≤50 years, Cushing's syndrome, thyroid dysfunction, or hypogonadism. Chronic kidney disease (defined as eGFR <60 mL/min/1.73m^2), severe hepatic disease, or severe pulmonary disease. Any active cancer diagnosis. Rheumatoid arthritis or a history of cerebrovascular disease. Current use of glucocorticoids, bisphosphonates, thiazolidinediones, SGLT-2 inhibitors, vitamin D/calcium supplements, or estrogen therapy.

Data and sample collection

Data were obtained using structured questionnaires, patient interviews, clinical examinations, and laboratory tests. Fasting venous blood (5 mL) was drawn from each participant as follows: 4 mL into gel tubes (serum separation), and 1 mL into EDTA tubes. Serum samples were centrifuged at 3,000 rpm for 10 min, aliquoted, and stored at –20°C until analysis. Hemolyzed samples were discarded.

Laboratory analyses

Routine metabolic parameters were measured on automated platforms. Fasting glucose and the lipid profile including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very-low-density lipoprotein cholesterol (VLDL-C) were analyzed. Additional biochemical markers, including glycated hemoglobin (HbA1c), uric acid, and liver enzymes (ALT and AST), were assessed using a Cobas C111 analyzer (Roche Diagnostics, Mannheim, Germany).

Serum concentrations of the primary biomarkers of interest were quantified using commercial enzyme-linked immunosorbent assay (ELISA) kits following the manufacturer's protocols. Specifically, human Angiopoietin-like protein-4 (ANGPTL4) was measured using a quantitative sandwich ELISA kit (Cat. No. E3119Hu, Shanghai, China). The reported detection range for this assay was 15.6-1000 ng/mL, with intra-assay and inter-assay coefficients of variation (CV) of <8% and <10%, respectively. Human Caveolin-1 (Cav-1) levels were determined using a similar quantitative sandwich ELISA kit (Cat. No. E1727Hu, Shanghai, China). This assay had a detection range of 0.156-100 ng/mL, with intra-assay and inter-assay CVs of <8% and <10%, respectively.

Statistical analysis

Statistical evaluations were carried out using GraphPad Prism (version 9.4.1) and MedCalc (version 20). Results are expressed as mean ± SD. The normal distribution of data was firstly evaluated, between the MetS and control groups continuous variables (e.g., clinical parameters and expression levels of biomarkers) were compared using independent samples t-tests, while categorical variables (such as sex) by using chi-square tests. Within the MetS group, subgroup analysis (e.g., subjects with or without diabetes mellitus, dyslipidemia, obesity and sex) was performed using independent samples t-test as well. Receiver Operating Characteristic (ROC) curve analysis was performed to calculate the Area Under the Curve (AUC) and optimal cut-off values of ANGPTL4 and Caveolin-1 for diagnosis. The correlation analysis between continuous variables was tested by Pearson's coefficient. Additionally, the independent predictors of MetS were determined using binary logistic regression. All comparisons were two-sided and p-value <0.05 was considered as statistically significant.

Results

Baseline demographic, clinical and biomarker characteristics of the included subjects are presented in Table 1. Both the MetS patients (n=60) and control individuals (n=30)

were matched with respect to age, sex distribution, total cholesterol, LDL-C homeostasis model assessment of insulin resistance levels, liver function tests (ALT and AST), and uric acid concentration (all p > 0.05). Characteristic phenotypic profile was as expected in patients with MetS, presenting statistically higher mean levels of BMI, WC, fasting glycemia, HbA1c, TG and VLDL-C (p-value < 0.001) and with significantly decreased in HDL-C concentrations. Crucially, the concentrations of the investigated biomarkers were substantially elevated in the MetS group compared to controls, with ANGPTL4 (142.78 ± 22.53 vs. 69.29 ± 30.80 ng/mL, p-value < 0.001) and Caveolin-1 (16.12 ± 2.87 vs. 8.51 ± 1.59 ng/mL, p-value < 0.001) both showing marked increases.

The significance level p < 0.05, statistical tests (independent samples t-test for continuous variables, chi-square for categorical variables).

A comparison of the prevalence of key clinical situations according to standard cut-off values for diagnosis is presented in Table 2. The MetS group had significantly higher prevalences of obesity (45.0% vs 3.3%), impaired fasting glucose (30.0% vs 10.0%), diabetes (48.3% vs 0), and dyslipidemia (58.3% vs 13.3%) than controls, respectively. Additionally, a high ANGPTL4 level greater than the mean plus one standard deviation of control was significantly higher in MetS patients (76.7% vs.16.7%).

Stratified analysis of levels of the biomarker by MetS patient is shown in Table 3. Patients with diabetes (HbA1c ≥ 6.5%) had higher levels of ANGPTL4 than those without (153.1 ± 30.5 ng/ml vs. 141.2 ± 22.8 ng/ml; p-value =0.045), and patients with dyslipidemia had higher concentrations than normal subjects (152.8 ± 29 pg/ml vs. 136,8 ± 22,5 pg/mL; p-value =0,008). A considerable sex effect was evident for ANGPTL4, being also higher in female patients. Conversely, Caveolin-1 was not statistically different for any of the strataled subgroups (diabetes status, dyslipidemia, obesity and sex).

ROC analysis was performed to assess the diagnostic values of ANGPTL4 and Caveolin-1 for differentiation of patients with MetS from healthy subjects. Both biomarkers had a great ability to distinguish cases from controls with AUC values close to 1. The AUCs of ANGPTL4 and Caveolin-1 were 0.97 (95.0%CI: 0.92–0.99) and 0.99 (95.0%CI: 0.94–1.00), respectively, and both p-values 119.47 ng/mL and Caveolin-1 >10.93 ng/mL as cut-off, the sensitivity and specificity of both markers were 96.7% at predicting saMets, which indicated their strong discriminative power to distinguish individuals with MetS from those without MetS (Figure 1).

In the MetS patient group, a correlation matrix was built in order to assess associations among selected continuous variables. The study biomarkers ANGPTL4 and Caveolin-1 demonstrated significant positive correlations with serum triglyceride levels (r = 0.371, p-value = 0.009 and r = 0.413, p-value = 0.003, respectively). Furthermore, a significant positive correlation was found between ANGPTL4 and Caveolin-1 levels (r = 0.389, p-value = 0.005). Caveolin-1 also showed a weak positive correlation with BMI (r =

Table 1. Demographic, clinical, and biomarker characteristics of the study participants.

Characteristic		Control group (n=30)	MetS patients (n=60)	p-value
Demographic & Clinical				
Age (years)		58.33 ± 4.84	60.28 ± 7.62	0.20
Gender	Male	12 (40.0 %)	21 (35.0 %)	0.43
	Female	18 (60.0 %)	39 (65.0 %)	
BMI (kg/m²)		24.67 ± 2.55	29.18 ± 2.81	<0.001
Waist circumference (cm)		84.6 ± 2.55	98.8 ± 6.7	<0.001
Metabolic Parameters				
Fasting Blood Glucose (mg/dL)		80.90 ± 11.03	124.23 ± 44.11	<0.001
HbA1c (%)		5.22 ± 0.52	7.68 ± 2.15	<0.001
Total Cholesterol (mg/dL)		172.07 ± 32.37	171.15 ± 41.11	0.92
Triglycerides (mg/dL)		87.17 ± 30.10	164.85 ± 71.07	<0.001
HDL-C (mg/dL)		51.13 ± 7.84	40.37 ± 9.72	<0.001
LDL-C (mg/dL)		103.63 ± 27.77	99.15 ± 37.94	0.57
VLDL-C (mg/dL)		17.37 ± 5.90	33.00 ± 14.54	<0.001
Liver Function & Other				
ALT (U/L)		20.43 ± 5.68	20.60 ± 6.15	0.90
AST (U/L)		21.53 ± 6.19	19.37 ± 6.74	0.14
Uric Acid (mg/dL)		4.14 ± 1.46	4.39 ± 1.48	0.46
Study Biomarkers				
ANGPTL4 (ng/mL)		69.29 ± 30.80	142.78 ± 22.53	<0.001
Caveolin-1 (ng/mL)		8.51 ± 1.59	16.12 ± 2.87	<0.001

Table 2. Prevalence of Clinical Conditions by Group Based on Standard Cut-offs

Condition (Definition)	Patient group (n=60)	Control group (n=30)
Obesity (BMI ≥ 30)	27 (45.0%)	1 (3.3%)
Impaired Fasting Glucose (FBS 100-125 mg/dl)	18 (30.0%)	3 (10.0%)
Diabetes (FBS ≥126 mg/dl or HbA1c ≥6.5%)	29 (48.3%)	0 (0%)
Dyslipidemia (Triglycerides ≥150 mg/dl or HDL <40 mg/dl)	35 (58.3%)	4 (13.3%)
High ANGPTL4 (>Mean + 1SD of Controls)	46 (76.7%)	5 (16.7%)

Table 3. Stratified Analysis of ANGPTL4 and Caveolin-1 Levels by Metabolic Health Status in MetS

Subgroup	No.	ANGPTL4 (ng/ml)	p-value	Caveolin-1 (ng/ml)	p-value
By Diabetes FBS ≥126 mg/dl or HbA1c ≥6.5%)					
HbA1c ≥ 6.5%)	25	153.1 ± 30.5	0.045	17.1 ± 3.4	0.078
HbA1c < 6.5%)	35	141.2 ± 22.8		15.6 ± 2.7	
By Dyslipidemia (Triglycerides ≥150 mg/dl or HDL <40 mg/dl)					
With Dyslipidemia	35	152.8 ± 28.1	0.008	16.2 ± 3.2	0.65
Without Dyslipidemia	25	136.8 ± 22.5		15.8 ± 2.4	
By Obesity (BMI ≥ 30)					
Obese (BMI ≥30)	26	141.8 ± 24.3	0.210	15.8 ± 3.5	0.49
Non-Obese (BMI <30)	34	143.9 ± 21.3		16.7 ± 2.7	
By Gender					
Male	21	133.9 ± 12.9	0.025	16.5 ± 2.8	0.71
Female	39	145.8 ± 28.6		16.1 ± 3.2	

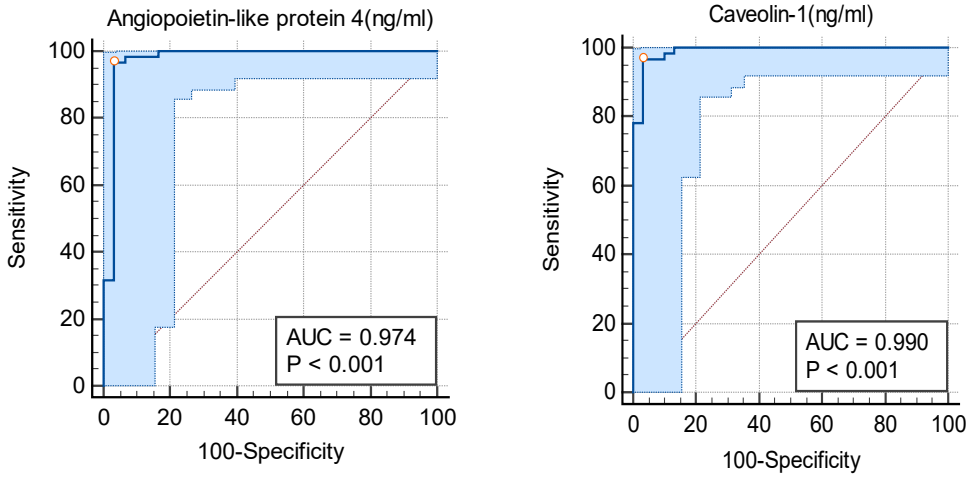

Fig. 1. ROC curve analysis of serum ANGPTL4 and Caveolin-1 for the diagnosis of MetS.

0.250, p-value = 0.046). Non-significant associations were observed for the other variables. For instance, fasting blood glucose showed a weak positive correlation with VLDL and triglycerides (r 0.32, p-value < 0.05), but not with the biomarkers. No other statistically significant correlations were observed between biomarkers and parameters such as LDL-C, HDL-C, HbA1c, or age (Figure 2).

Binary logistic regression analysis (Table 4) identified ANGPTL4 and Caveolin-1 as significant independent predictors of MetS status after adjusting for triglycerides, which was the only conventional lipid parameter retained in the model. For each one-unit increase in ANGPTL4 (ng/mL), the odds of having MetS increased by 23.0% (OR = 1.23, 95.0% CI, 1.062–1.446; p-value =0.006). A one-unit increase in Caveolin-1 (ng/mL) was associated with a more than fourfold increase in the odds of MetS (OR = 4.23, 95.0% CI: 1.92–9.32, p-value <0.001). The overall model was highly significant (χ^2 = 11.26, p-value < 0.001) and explained a substantial proportion of the variance in MetS status (Nagelkerke's R^2 = 0.91).

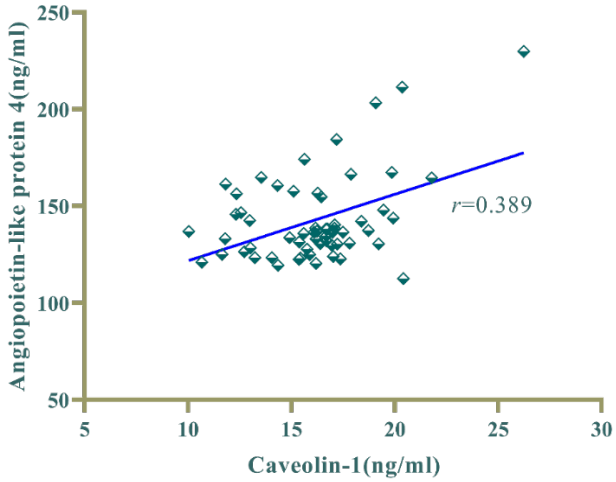

Fig. 2. Correlation matrix of metabolic parameters and novel biomarkers in the MetS.

Table 4: Binary Logistic Regression Identifies ANGPTL4 and Caveolin-1 as Independent Predictors of MetS

Predictor	B	S.E.	Wald	p-value	Odds Ratio (OR)	95% CI for OR
ANGPTL4	0.21	0.078	7.4	0.006	1.23	(1.062 to 1.446)
Caveolin-1	1.44	0.4	12.8	<0.001	4.23	(1.92 to 9.32)
HbA1c (%)	Variable not included in the model					
Total Cholesterol	Variable not included in the model					
Triglycerides	0.04	0.023	4.19	0.04	1.049	(1.002 to 1.098)
HDL-C	Variable not included in the model					
LDL-C	Variable not included in the model					
Constant	-15.95	4.46	12.76	0.0004	-	-

Dependent Variable: Group (MetS = 1, Combined Controls = 0). Model $\chi^2 = 11.26$, $p < 0.001$, Nagelkerke $R^2 = 0.91$.

Discussion

This study demonstrated the significant potential of serum ANGPTL4 and Caveolin-1 levels as novel diagnostic biomarkers for metabolic syndrome in Iraqi adults over 50 years of age. The most striking finding was the exceptional diagnostic performance of both biomarkers, with ANGPTL4 achieving an AUC of 0.974 (sensitivity, 96.6%; specificity, 93.3%) and Caveolin-1 demonstrating even higher performance with an AUC of 0.990 (sensitivity, 96.6%; specificity, 96.6%). These results represent a substantial advancement over traditional MetS diagnostic approaches, and suggest that these biomarkers could significantly enhance early detection.

The elevated concentrations of ANGPTL4 in patients with MetS are consistent with its established role in lipid metabolism. As a potent inhibitor of LPL, ANGPTL4 directly contributes to the hypertriglyceridemia characteristic of MetS by reducing triglyceride clearance [10,15]. Our findings align with previous reports [16] and are further supported by evidence that ANGPTL4 expression is regulated by metabolic states, including fasting and insulin resistance. Its multifaceted role in lipid metabolism, inflammation, and vascular permeability makes it a compelling biomarker that reflects the complex pathophysiology of MetS [15,17].

Similarly, the marked increase in Caveolin-1 levels observed in the MetS group reflects fundamental alterations in cellular signaling and membrane structure. A result is similar to that reported by Arefian et al. [18]. Caveolin-1 is a critical scaffolding protein essential for cholesterol homeostasis, insulin signaling, and lipid metabolism [19,20]. Dysregulation of Caveolin-1 is linked to the core components of MetS, including insulin resistance and endothelial dysfunction. This clinical observation is corroborated by genetic studies demonstrating that certain CAV1 variants are associated with an increased risk of MetS in various populations, thereby providing a genetic basis for its role in metabolic dysfunction [21,22].

The results of this study show that serum ANGPTL4 and Caveolin-1 are highly useful as novel candidate MetS diagnostic markers in those over 50 years old. After discarding false positives due to overlap between individuals, the present study demonstrated that Caveolin-1 and ANGPTL4 exhibited diagnostic accuracy, with AUC values of 0.990 and 0.974, respectively. These values approach the threshold for clinical utility in routine diagnostic practice and compare favorably with previously reported biomarkers for MetS [23].

While conventional criteria are essential for diagnosis, they often identify MetS at a relatively late stage. The introduction of biomarkers such as ANGPTL4 and Caveolin-1 may facilitate a shift towards more proactive and personalized management of MetS [24]. By reflecting key pathophysiological processes like lipid dysregulation and endothelial dysfunction, these markers have the potential to serve as early indicators of metabolic distress, allowing for timely intervention before the full clinical onset of the syndrome [25,26]. Furthermore, they may enable more nuanced risk stratification beyond traditional clinical assessments, helping to distinguish between patients with different underlying molecular pathologies[27]. This approach aligns with the principles of precision medicine, where biomarkers could guide more targeted therapeutic strategies [28]. Therefore, while not replacing cost-effective clinical criteria, ANGPTL4 and Caveolin-1 could serve as valuable second-line tools for early detection and risk assessment in high-risk populations.

The observed biomarker elevations occurred within the broader context of insulin resistance, which is the central pathophysiological mechanism underlying MetS. The significant differences in fasting blood glucose and HbA1c levels between the patient and control groups in this study reflect the progressive insulin resistance that characterizes this condition. Both ANGPTL4 and Caveolin-1 intersect with insulin signaling pathways, with ANGPTL4 contributing to lipid-mediated insulin resistance through its effects on free fatty acid availability, while Caveolin-1 directly participates in insulin receptor signaling and glucose metabolism [29,30]. The chronic low-grade inflammation characteristic of MetS provides additional mechanistic evidence for these biomarkers. ANGPTL4 involvement in inflammatory processes, particularly oxidative stress and chronic inflammation, aligns with the inflammatory milieu observed in patients with MetS. Similarly, Caveolin-1 role in organizing cholesterol-rich membrane microdomains affects inflammatory signaling pathways and cellular responses to metabolic stress [23,29,31].

Conventional diagnosis of metabolic syndrome is based on clinical factors like waist circumference, blood pressure, fasting glucose level, triglycerides and HDL cholesterol. While these criteria are still necessary, they often do not catch MetS in early stages and do not encompass its

underlying pathophysiological heterogeneity. Clinical applications It may be speculated that the introduction of ANGPTL4 and Caveolin-1 as diagnostic markers would improve early detection and monitoring [27,32].

Focusing on a population aged 50 years and older is particularly relevant, as the prevalence of MetS increases significantly with age, affecting over 40% of individuals in this demographic. Age-related changes in metabolic regulation, including decreased insulin sensitivity and altered lipid metabolism, create a pathophysiological environment where ANGPTL4 and Caveolin-1 dysregulation is especially pertinent [33,34]. This age-specific approach addresses the clinical reality that MetS in older adults confers a higher risk of adverse cardiovascular outcomes, making early and accurate detection critical for implementing preventive strategies [34,35].

Strengths and Limitations

The main strengths of this study are the comprehensive statistical approach and the excellent diagnostic value for both markers. ROC analysis was used, supplemented by robust estimation of the AUC, to demonstrate excellent clinical discrimination. The age-matched design reduces potential confounding by age-related metabolic changes, and the emphasis on subjects 50 yr of age (or older) addresses a high-risk population in which early detection is most useful. Nevertheless, there are some limitations to this study. The inherent limitations of the relatively small sample size that may affect the generalizability as well as the limitation for biomarkers validation, in addition to a cross-sectional single-centered design confined to Iraq adults older than 50 years prevented us from elaborating insights in relation to biodynamic of these biomarkers over time (e.g., tracking disease progression or treatment response) and limited their applicability for other ethnicities, younger individuals or different care settings which was con- firmed by Caveolin-1 variants racial specific association with MetS. Hence, further large longitudinal studies in the other populations are necessary to validate the value of biomarkers for monitoring, prognosis and more extended clinical practice.

Conclusion

This study provides compelling evidence for the exceptional diagnostic utility of serum ANGPTL4 and Caveolin-1 levels as novel biomarkers for MetS in adults over 50 years of age. The mechanistic basis for their dysregulation in MetS and the excellent diagnostic performance of such biomarkers make them promising candidates to become transformative tools for early diagnosis and clinical practice. These results warrant future exploration of these markers in the context of larger and more diverse populations and their inclusion in comprehensive diagnostic and therapeutic strategies for MetS. The prognostic implications of these findings in different populations and by strategy to improve method standardization are subjects for further investigation.

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Authors' Contributions

HIA: Conceptualization, Methodology, Investigation, Data Curation, writing – Original Draft, Visualization, Formal Analysis, Software, Validation, Writing – Review & Editing. ERS: Supervision, Project Administration, Resources, Conceptualization, Writing, Review & Editing.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available because of participant privacy and confidentiality concerns but are available from the corresponding author upon reasonable request.

Conflict of interest

None to declare.

Ethical approval

An agreement to conduct this study was signed before sample collection began. The Tikrit University College of Medicine collaborated in this study. This study was approved by the research committee (No. 3/3/2025) in accordance with the Declaration of Helsinki. All participants provided written informed consent to participate in the study.

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