Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Obesity-Associated Adipokine Dysregulation in Adults with Type 2 Diabetes Mellitus: A Cross-Sectional Study

Abid Shaheer

abidshaheer@gmail.com

Gulf Medical University

Mahir Jallo

Thumbay University Hospital

Ashok Kumar

Rajah Muthaiah Medical College, Annamalai University

Research Article

Keywords: Adipokines, adiponectin, FABP4, RBP4, visfatin, obesity, type 2 diabetes mellitus, sex differences

Posted Date: July 31st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10233010/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Obesity contributes to metabolic heterogeneity in type 2 diabetes mellitus (T2DM), but conventional glycemic and lipid markers may not fully capture obesity-related adipose tissue dysfunction. Circulating adipokines may provide additional insight into adipose endocrine dysregulation in individuals with T2DM. This study evaluated differences in circulating retinol-binding protein 4 (RBP4), fatty acid-binding protein 4 (FABP4), visfatin, and adiponectin between overweight and obese adults with T2DM, with exploratory assessment of sex-stratified patterns.

Methods

This cross-sectional study included 100 adults with established T2DM who were classified as overweight (body mass index [BMI] 25.0–29.9 kg/m²; n = 50) or obese (BMI ≥ 30.0 kg/m²; n = 50). Participants were further stratified by sex into overweight males (n = 32), overweight females (n = 18), obese males (n = 41), and obese females (n = 9). Serum RBP4, FABP4, visfatin, and adiponectin concentrations were measured using enzyme-linked immunosorbent assays. Group differences were assessed using two-way linear models evaluating BMI category, sex, and BMI category × sex interaction effects.

Results

Glycemic indices and lipid parameters were broadly comparable across BMI and sex strata. In contrast, obesity was associated with significantly higher circulating RBP4, FABP4, and visfatin concentrations and significantly lower adiponectin concentrations compared with overweight status. BMI category showed significant main effects for all four adipokines. No significant BMI category × sex interactions were observed for RBP4, FABP4, or visfatin. Adiponectin showed a significant BMI category × sex interaction, suggesting a possible greater obesity-associated reduction among females; however, this finding should be interpreted as exploratory because of the small obese female subgroup.

Conclusions

Among adults with T2DM, obesity was associated with coordinated alterations in circulating adipokines despite broadly similar routine glycemic and lipid profiles. These findings suggest that adipokine profiling may reflect obesity-related adipose tissue dysfunction not captured by conventional metabolic markers. The observed sex-related adiponectin pattern is hypothesis-generating and requires confirmation in larger, sex-balanced longitudinal cohorts incorporating direct or validated surrogate measures of visceral adiposity and insulin resistance.

1. Background

Type 2 diabetes mellitus (T2DM) is one of the most important contributors to global cardiometabolic morbidity, with recent estimates indicating a continued rise in disease prevalence and treatment burden worldwide [1]. This increasing burden has occurred in parallel with the global escalation of overweight and obesity, which substantially influence the development, progression, and clinical heterogeneity of T2DM [2]. Population-level projections further suggest a continuing shift toward higher body mass index (BMI) distributions, reinforcing the need to better characterize obesity-related biological pathways in individuals with established T2DM [3].

Contemporary diabetes care increasingly emphasizes comprehensive cardiometabolic risk reduction, including attention to weight-related comorbidities and obesity-associated complications [4]. However, BMI alone provides an incomplete assessment of metabolic risk because it does not distinguish between fat mass and lean mass, nor does it directly reflect adipose tissue distribution, ectopic lipid accumulation, or adipose tissue dysfunction [5]. Visceral adipose tissue is particularly relevant in this context, as excess visceral fat is closely linked to insulin resistance, inflammatory signalling, and adverse cardiometabolic outcomes in patients with T2DM [6].

Although direct quantification of visceral adipose tissue using imaging methods is informative, it is not always feasible in routine clinical or resource-limited research settings. Therefore, anthropometric and biochemical surrogates of visceral adiposity have gained increasing attention in metabolic risk phenotyping [7]. Evidence from systematic reviews and meta-analyses supports the use of the visceral adiposity index as a predictor of T2DM risk, suggesting that visceral adiposity-related measures may provide information beyond BMI alone [8]. Additional prospective and population-based studies have also shown that visceral obesity indices are associated with future diabetes risk and adverse glycemic profiles in diverse populations [9, 10]. These findings support the broader concept that obesity-related risk in T2DM is not determined solely by body size but also by the functional and endocrine status of adipose tissue.

Adipose tissue is now recognized as an active endocrine and immune-metabolic organ rather than a passive site of energy storage. In obesity, adipocyte hypertrophy, impaired lipid handling, hypoxia, oxidative stress, and immune cell infiltration contribute to adipose tissue dysfunction [11]. The concept of adiposopathy describes the pathophysiological state in which dysfunctional adipose tissue promotes insulin resistance, systemic inflammation, and cardiometabolic complications [12]. Therefore, inflammatory remodeling of adipose tissue is considered a central mechanism linking obesity with insulin resistance and T2DM progression [13]. Beyond local tissue effects, adipose-derived mediators exert systemic actions on hepatic, vascular, skeletal muscle, and pancreatic pathways, making circulating adipokines biologogically plausible markers of obesity-related metabolic dysfunction [14].

The metabolic consequences of adipose tissue dysfunction are closely related to lipid overflow, ectopic fat deposition, and the progressive impairment of insulin-sensitive tissues [15]. Importantly, these processes may differ by sex because biological differences in fat distribution, adipose tissue expandability, sex hormone signalling, and substrate metabolism influence cardiometabolic risks [16]. Therefore, sex-related variations in adipose tissue biology may affect both adipokine secretion and the metabolic response to increasing adiposity [17]. Experimental and clinical evidence indicates that adipose remodeling, energy metabolism, and inflammatory adaptation differ between men and women [18, 19]. Furthermore, sex

differences in regional fat distribution are associated with distinct patterns of susceptibility to diabetes and metabolic risk [20]. Recent analyses also suggest that insulin resistance and obesity-related metabolic deterioration may follow sex-specific trajectories [21], whereas adipose tissue signatures in obesity and T2DM appear to differ according to sex [22]. These observations support the importance of considering sex-stratified patterns when evaluating endocrine dysfunction in T2DM.

Circulating adipokines provide a measurable endocrine readout of adipose tissue function and may capture obesity-associated biological alterations that are not fully reflected by routine glycemic and lipid parameters [23]. Adipokines also influence pancreatic β-cell function, inflammatory pathways, vascular biology, and insulin sensitivity, indicating their potential relevance to the progression and complication profile of T2DM [24]. Among these biomarkers, adiponectin is generally considered protective because of its insulin-sensitizing, anti-inflammatory, and vasculoprotective effects, although context-dependent paradoxical associations have been described in some clinical populations [25]. Genetic and population-level data further support the role of adiponectin pathways in obesity- and T2DM-related phenotypes [26]. Interventional and bariatric surgery studies have also demonstrated that improvements in metabolic status and reductions in adiposity are often accompanied by favorable changes in adiponectin concentrations [27, 28].

In contrast, retinol-binding protein 4 (RBP4), fatty acid-binding protein 4 (FABP4), and visfatin are generally associated with adverse metabolic states. RBP4 has been implicated in obesity-related insulin resistance and adipose hepatic metabolic dysfunction [29]. FABP4, an adipocyte- and macrophage-derived lipid-binding protein, is increasingly recognized as a marker and mediator of adipose tissue stress, lipid dysregulation, inflammation, and cardiometabolic risk factors. [30]. Visfatin has also been linked to inflammatory-metabolic signalling in obesity-related disorders, although its clinical interpretation remains heterogeneous across studies [31]. Conversely, adiponectin may serve as a complementary marker for refining cardiometabolic risk assessment in T2DM beyond anthropometric indices alone [32].

Despite growing evidence linking adipokines with obesity and T2DM, little is known about whether circulating adipokine profiles differ between overweight and obese adults with established T2DM when routine glycemic and lipid indices are broadly comparable. In addition, the extent to which these adipokine patterns vary by sex in clinically managed T2DM populations remains insufficiently characterized. Addressing this gap may help clarify whether adipokine profiling provides additional biological information on obesity-related adipose tissue dysfunction beyond conventional clinical markers.

The novelty of the present study lies in evaluating whether a coordinated adipokine signature distinguishes obese from overweight adults with established T2DM despite broadly comparable routine glycemic and lipid indices. This approach may help clarify whether adipokine profiling provides biological information on adipose tissue dysfunction beyond conventional metabolic markers in clinically managed T2DM populations. Therefore, the present study aimed to evaluate the circulating levels of RBP4, FABP4, visfatin, and adiponectin in overweight and obese adults with T2DM. A secondary exploratory objective was to examine whether these adipokine patterns differed by sex, with particular attention to obesity-associated differences that may not be captured by routine glycemic and lipid measurements.

2. Methods

2.1 Study Design and Setting

This cross-sectional observational study was conducted among adults with T2DM who attended Thumbay University Hospital in Ajman, United Arab Emirates. The objective was to evaluate variations in circulating adipokine profiles according to adiposity status and to explore potential sex-based differences in these patterns. The study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies. Participants were consecutively recruited from among eligible patients attending the hospital. They were classified according to BMI into two predefined adiposity categories: overweight and obese. A secondary exploratory analysis was performed after stratification by sex.

2.2 Study Participants

A total of 100 adults with T2DM were enrolled in this study. Participants were classified into overweight and obese groups according to their BMI. The overweight group included participants with BMI of 25.0–29.9 kg/m², while the obese group included participants with BMI ≥ 30.0 kg/m². Each group comprised 50 participants.

For sex-stratified analyses, participants were categorized into four subgroups: overweight males, overweight females, obese males, and obese females. The subgroup distribution was as follows: overweight males, n = 32; overweight females, n = 18; obese males, n = 41; and obese females, n = 9.

The diagnosis of T2DM was confirmed using clinical records. Eligible participants were adults aged 30–60 years with established T2DM and available anthropometric, biochemical, and adipokine data.

2.3 Inclusion and Exclusion Criteria

Participants were included if they were aged 30–60 years, had a confirmed diagnosis of T2DM, had BMI values within the overweight or obese range, and provided written informed consent before enrolment.

Participants were excluded if they had acute illness, known inflammatory disorders, endocrine disorders other than T2DM, pregnancy, documented chronic liver disease, documented chronic kidney disease, or incomplete clinical, anthropometric, biochemical, or adipokine data required for the primary analysis.

2.3 Anthropometric and Clinical Measurements

Anthropometric measurements were performed using standardized procedures. Body weight was measured with the participants wearing light clothing and no footwear. Height was measured using a calibrated stadiometer. BMI was calculated as body weight in kilograms divided by height in meters squared. Waist circumference was measured using a non-stretchable measuring tape at the midpoint between the lower margin of the last palpable rib and the upper border of the iliac crest. The measurements were recorded in centimeters. Blood pressure was measured in the seated position after an adequate resting period using a calibrated sphygmomanometer. Systolic and diastolic blood pressure values were recorded in mmHg. Sex was recorded as male or female based on clinical records. Because gender identity was not assessed separately, the analysis is described as sex-stratified rather than gender-stratified.

2.4 Biochemical Measurements

Venous blood samples were collected after overnight fasting. Fasting blood glucose, postprandial blood glucose, glycated hemoglobin (HbA1c), and lipid profile parameters were measured using standard automated clinical chemistry methods, according to routine laboratory protocols. The lipid profile included total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, and total cholesterol/high-density lipoprotein cholesterol ratio.

Renal function markers, including urea and creatinine levels, were measured using routine automated biochemical methods. Liver enzymes, including alanine aminotransferase and aspartate aminotransferase, were also evaluated. Serum total protein, albumin, globulin, and albumin-to-globulin ratio were measured as routine biochemical parameters.

2.5 Adipokine Measurements

Serum concentrations of retinol-binding protein 4 (RBP4), fatty acid-binding protein 4 (FABP4), visfatin, and adiponectin were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits (BioVendor Laboratorní medicína, Czech Republic), according to the manufacturer's instructions.

Serum RBP4 was estimated using a competitive ELISA method for the quantitative determination of human RBP4. Serum FABP4 levels were estimated using a sandwich ELISA method based on wells coated with polyclonal anti-human FABP antibodies. Serum visfatin levels were measured using a sandwich ELISA method based on monoclonal antibody-coated wells specific for human visfatin. Serum adiponectin levels were measured using an ELISA method based on wells coated with human adiponectin antigen and horseradish peroxidase-conjugated anti-human adiponectin antibodies.

All serum samples, standards, and quality controls were analyzed in duplicates. Standard curves were generated by plotting the absorbance values of the standards against their known concentrations, and the sample concentrations were calculated from the corresponding standard curve. The final concentrations were corrected for dilution factors, where applicable.

Tetramethylbenzidine was used as the chromogenic substrate, and the reaction was terminated using stop solution. Absorbance was measured using a microplate reader (Sunrise; Tecan Group Limited). RBP4 absorbance was read at 450 nm with a reference wavelength of 540 nm. FABP4 and adiponectin absorbance were measured at 450 nm with a reference wavelength of 630 nm. Visfatin absorbance was measured at 450 nm.

Adipokine concentrations were reported as µg/mL for RBP4 and adiponectin and ng/mL for FABP4 and visfatin. The reference intervals provided in the manufacturer's package inserts were 10–70 µg/mL for RBP4, 2–46 ng/mL for FABP4, 0.2–1.5 ng/mL for visfatin, and 4.5–22 µg/mL for adiponectin.

Quality control procedures were applied throughout the assay process, including duplicate analysis of samples, standards, and controls, use of standard curves for concentration calculation, and adherence to the manufacturer-recommended incubation, washing, substrate reaction, and absorbance-reading procedures.

2.6 Clinical covariates and potential confounders

Available clinical and laboratory variables included age, sex, BMI, waist circumference, blood pressure, fasting blood glucose, postprandial blood glucose, HbA1c, lipid profile, renal function markers, liver enzymes, and serum protein parameters. Data on diabetes duration, medication use, smoking status, menopausal status, physical activity, and dietary intake were not available for incorporation into adjusted models; therefore, these variables were considered potential unmeasured confounders and are addressed as limitations.

2.7 Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables are summarized as mean ± standard deviation. Categorical variables were summarized using frequencies and percentages. The participants were analyzed according to BMI category and sex. Group comparisons were performed using two-way linear models with BMI category, sex, and BMI category × sex interaction as the fixed factors. The main effects of BMI category and sex were evaluated, and the interaction term was used to assess whether the association between the BMI category and each outcome differed between males and females.

Separate two-way linear models were constructed for anthropometric variables, blood pressure, glycemic indices, lipid parameters, renal function markers, liver enzymes, serum proteins, and adipokines. For the primary adipokine analysis, RBP4, FABP4, visfatin, and adiponectin were evaluated as the dependent variables in separate models. Statistical significance was set at $p < 0.05$. Interaction findings were interpreted cautiously, particularly when subgroup sample sizes were small. Distribution-level differences in adipokines across the BMI-sex strata were visualized using box-and-whisker plots to assess median shifts, interquartile ranges, variability, and potential outliers across subgroups.

2.8 Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Board of the Gulf Medical University, Ajman, United Arab Emirates (Approval No. IRB/COM/FAC/05/2018). Written informed consent was obtained from all participants prior to enrolment. All study procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki and its subsequent amendments.

3. Results

3.1 Study population and baseline characteristics

A total of 100 adults with type 2 diabetes mellitus (T2DM) were included in the analysis. Participants were classified into overweight (n = 50) and obese (n = 50) groups and further stratified by sex into overweight males (n = 32), overweight females (n = 18), obese males (n = 41), and obese females (n = 9). The baseline demographic and anthropometric characteristics are presented in Table 1. Age did not differ significantly according to BMI category, sex, or BMI category × sex interaction. As expected, body weight, BMI, and waist circumference were significantly higher in obese participants than in overweight participants, confirming a

clear anthropometric separation between the two adiposity groups. Body weight also showed a significant sex effect, whereas BMI did not differ significantly by sex.

Waist circumference increased significantly with obesity in the study population. Although the effect of sex on waist circumference approached statistical significance, the BMI category × sex interaction was not significant. Systolic blood pressure did not show a significant main effect of BMI category or sex; however, a significant BMI category × sex interaction was observed. This interaction appeared to reflect lower systolic blood pressure among obese females than among obese males, whereas values were broadly similar between overweight males and females. Given the small number of obese female participants, this finding should be interpreted with caution. Diastolic blood pressure did not differ significantly according to BMI category, sex, or their interactions.

Table 1
Demographic and anthropometric characteristics stratified by Sex and BMI category

Variable	Overweight, Male (n = 32)	Overweight, Female (n = 18)	Obese, Male (n = 41)	Obese, Female (n = 9)	p (BMI category)	p (Sex)	p (Interaction)
Age, y	48.00 ± 7.46	45.61 ± 7.13	44.07 ± 7.48	47.00 ± 8.25	0.092	0.856	0.135
Weight, kg	76.18 ± 7.58	80.87 ± 9.16	87.74 ± 9.72	91.91 ± 6.53	< .001	0.028	0.901
BMI, kg/m²	27.66 ± 1.19	26.97 ± 1.55	32.13 ± 1.36	31.84 ± 1.01	< .001	0.081	0.515
Waist circumference, cm	95.92 ± 4.35	96.48 ± 1.74	98.69 ± 4.70	102.47 ± 2.34	< .001	0.053	0.094
Systolic BP, mmHg	120.00 ± 8.80	122.06 ± 7.94	122.68 ± 8.67	116.11 ± 7.82	0.764	0.504	0.034
Diastolic BP, mmHg	75.00 ± 5.68	77.11 ± 7.33	77.80 ± 6.13	75.56 ± 5.27	0.176	0.774	0.136

Data are presented as mean ± standard deviation (SD). p values were obtained from a 2-way linear model (BMI category × sex), reporting the main effects and the interaction term. Abbreviations: BMI, body mass index; BP, blood pressure; SD, standard deviation; T2DM, type 2 diabetes mellitus; y, years.

3.2 Glycemic indices and lipid profile

Across the four sex-BMI strata, the glycemic indices were highly comparable (Table 2). Fasting blood glucose, postprandial blood glucose, and HbA1c showed no significant BMI-category main effect, no significant sex main effect, and no interaction, indicating that overweight versus obesity was not associated with measurable differences in glycemic control within this cohort. Likewise, the lipid profile (total cholesterol, triglycerides, HDL, LDL, VLDL, and TC/HDL ratio) showed no significant differences by BMI category or sex, and no interaction effects. This overall metabolic similarity provides an important context for

interpreting adipokines: the primary biological separation between overweight and obese T2DM participants in this dataset is not captured by routine glycemic or lipid indices.

Table 2
Glycemic indices and lipid profile stratified by Sex and BMI category

Variable	Overweight, Male (n = 32)	Overweight, Female (n = 18)	Obese, Male (n = 41)	Obese, Female (n = 9)	p (BMI category)	p (Sex)	p (Interaction)
Fasting blood glucose, mmol/L	13.75 ± 1.11	13.54 ± 0.94	13.75 ± 0.96	13.53 ± 1.32	1.000	0.381	0.976
Postprandial blood glucose, mmol/L	18.79 ± 1.49	18.74 ± 1.36	18.49 ± 1.08	17.80 ± 0.98	0.079	0.309	0.283
HbA1c, %	9.31 ± 0.40	9.25 ± 0.44	9.26 ± 0.35	9.27 ± 0.56	0.715	0.709	0.744
Total cholesterol, mmol/L	5.36 ± 0.30	5.30 ± 0.27	5.44 ± 0.31	5.34 ± 0.24	0.222	0.274	0.775
Triglycerides, mmol/L	2.20 ± 0.15	2.18 ± 0.13	2.20 ± 0.17	2.14 ± 0.15	0.827	0.282	0.636
VLDL cholesterol, mmol/L	1.02 ± 0.06	0.99 ± 0.05	1.02 ± 0.07	0.99 ± 0.08	0.838	0.080	0.897
HDL cholesterol, mmol/L	1.19 ± 0.09	1.17 ± 0.08	1.19 ± 0.08	1.17 ± 0.07	0.752	0.332	0.994
LDL cholesterol, mmol/L	3.16 ± 0.33	3.11 ± 0.32	3.24 ± 0.30	3.20 ± 0.23	0.179	0.519	0.936
TC/HDL ratio	4.53 ± 0.47	4.55 ± 0.47	4.63 ± 0.45	4.59 ± 0.39	0.397	0.960	0.803

Data are presented as the mean ± SD. p values were obtained from a 2-way linear model (BMI category × gender). Abbreviations: HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides; VLDL, very low-density lipoprotein; SD, standard deviation.

3.3 Renal function, liver enzymes and serum proteins

Renal and hepatic markers were broadly stable across the BMI categories and sex strata (Table 3). Urea showed a significant BMI category main effect (p = .005), which was modestly higher in patients with obesity in both males and females. Notably, creatinine levels did not differ significantly, suggesting that urea

elevation is unlikely to reflect overt renal impairment and may be influenced by hydration status, dietary protein intake, early renal hemodynamics, or medication effects. Liver enzymes were generally similar; however, ALT demonstrated a significant BMI category × gender interaction (p = .034), indicating that the obesity-associated ALT pattern differed by sex. This interaction appears to be driven by lower ALT levels among obese females than among obese males, whereas ALT values were similar between overweight males and females. Given the small subgroup of obese females, this observation should be interpreted cautiously. Serum protein levels did not differ significantly, suggesting no major differences in routine protein indices across the strata.

Table 3
Renal function, liver enzymes and serum proteins stratified by Sex and BMI category

Variable	Overweight, Male (n = 32)	Overweight, Female (n = 18)	Obese, Male (n = 41)	Obese, Female (n = 9)	p (BMI category)	p (Sex)	p (Interaction)
Urea, mmol/L	4.04 ± 0.78	4.17 ± 0.73	4.55 ± 0.72	4.41 ± 0.81	0.005	0.890	0.463
Creatinine, μmol/L	93.41 ± 17.90	96.28 ± 15.36	90.17 ± 20.92	93.44 ± 18.18	0.417	0.486	0.964
Total protein, g/L	70.41 ± 3.85	71.06 ± 4.70	70.88 ± 4.91	71.44 ± 4.36	0.625	0.553	0.969
Albumin, g/L	45.06 ± 3.17	45.28 ± 3.08	45.37 ± 3.40	45.00 ± 3.39	0.814	0.988	0.707
Globulins, g/L	25.34 ± 3.14	25.78 ± 3.32	25.51 ± 2.71	26.44 ± 2.30	0.626	0.355	0.720
A/G ratio	1.81 ± 0.32	1.77 ± 0.28	1.80 ± 0.19	1.70 ± 0.19	0.551	0.295	0.649
AST, U/L	31.47 ± 7.92	30.33 ± 6.41	30.41 ± 6.45	30.33 ± 7.07	0.582	0.654	0.750
ALT, U/L	26.03 ± 5.41	26.17 ± 3.47	26.59 ± 5.57	21.22 ± 7.64	0.460	0.110	0.034

Data are presented as the mean ± SD. p values were obtained from a 2-way linear model (BMI category × gender). Abbreviations: A/G, albumin/globulin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SD, standard deviation; U/L, units per liter.

3.4 Adipokines

The serum adipokine concentrations are presented in Table 4 and illustrated in Fig. 1. The BMI category showed significant main effects for all four adipokines. Compared with overweight participants, obese participants had significantly higher circulating concentrations of RBP4, FABP4, and visfatin and significantly lower adiponectin concentrations. RBP4 concentrations were higher in both obese males and females than in their overweight counterparts. The sex main effect and BMI category × sex interaction were not statistically

significant for RBP4, indicating that the obesity-associated increase was broadly consistent across men and women.

FABP4 concentrations also significantly increased with obesity. Both obese males and females showed higher FABP4 levels than overweight males and females. No significant sex main effect or BMI category × sex interaction was observed, suggesting that the BMI category was the principal determinant of FABP4 variation in this cohort. Visfatin concentrations were significantly higher in obese participants than in overweight participants. Similar to RBP4 and FABP4, visfatin did not show a significant sex main effect or BMI category × sex interaction, indicating a consistent obesity-associated increase across sex strata.

Adiponectin showed the opposite pattern, with significantly lower concentrations among obese participants compared with overweight participants. In contrast to other adipokines, adiponectin levels demonstrated a significant BMI category × sex interaction. Overweight males and females had comparable adiponectin levels, whereas obese females had lower adiponectin concentrations than obese males. This finding suggests a potentially greater obesity-associated reduction in adiponectin levels among females; however, it should be interpreted cautiously because of the small number of obese female participants.

Table 4
Adipokines stratified by Sex and BMI category

Adipokine	Overweight, Male (n = 32)	Overweight, Female (n = 18)	Obese, Male (n = 41)	Obese, Female (n = 9)	p (BMI category)	p (Sex)	p (Interaction)
RBP4, µg/mL	96.19 ± 10.74	91.83 ± 12.77	125.02 ± 13.26	127.78 ± 8.50	< .001	0.570	0.214
FABP4, ng/mL	46.36 ± 3.84	43.92 ± 4.58	56.05 ± 4.94	56.62 ± 4.43	< .001	0.225	0.160
Visfatin, ng/mL	8.68 ± 0.86	8.17 ± 1.02	11.59 ± 1.28	11.91 ± 0.90	< .001	0.463	0.108
Adiponectin, µg/mL	10.43 ± 1.93	10.49 ± 1.92	7.14 ± 2.22	5.07 ± 1.14	< .001	0.096	0.027

Data are presented as the mean ± SD. p values were obtained from a 2-way linear model (BMI category × gender). Adipokines were measured by enzyme-linked immunosorbent assay (ELISA) per protocol. Abbreviations: ELISA, enzyme-linked immunosorbent assay; FABP4, fatty acid-binding protein 4; RBP4, retinol-binding protein 4; SD, standard deviation; T2DM, type 2 diabetes mellitus.

Overall, Fig. 1 reinforces that adipokines (RBP4, FABP4, visfatin, and adiponectin) sharply differentiate overweight from obese T2DM participants, even when HbA1c, fasting/postprandial glucose, and standard lipid measures remain similar between BMI categories.

In this cohort of adults with T2DM, obesity was associated with higher body weight, BMI, and waist circumference, whereas routine glycemic and lipid parameters remained broadly comparable between overweight and obese participants. Renal, hepatic, and serum protein markers were largely similar across

groups, except for higher urea levels in obesity and exploratory interaction effects of systolic blood pressure and alanine aminotransferase.

The most consistent biological differences were observed in the adipokine panel. Obesity was associated with elevated RBP4, FABP4, and visfatin levels and reduced adiponectin levels. These adipokine alterations were observed despite broadly similar HbA1c, glucose, and lipid profiles in the two groups. The adiponectin interaction by BMI category and sex suggests a possible sex-related difference in the adipose endocrine response to obesity; however, this finding should be regarded as hypothesis-generating because of the small obese female subgroup.

4. Discussion

The present study demonstrated that obesity is associated with a distinct circulating adipokine profile among adults with type 2 diabetes mellitus (T2DM), despite broadly comparable glycemic and lipid indices between overweight and obese participants. Although the two BMI categories were clearly separated by anthropometric measures, fasting blood glucose, postprandial blood glucose, HbA1c, and lipid profile parameters did not differ significantly across the BMI and sex strata. In contrast, circulating RBP4, FABP4, and visfatin concentrations were significantly higher, whereas adiponectin concentrations were significantly lower in obese participants. These findings suggest that adipokine alterations may reflect obesity-related adipose tissue dysfunction in T2DM, even when conventional metabolic markers appear similar.

The dissociation between routine biochemical markers and adipokine profiles is clinically significant. In treated T2DM populations, glycemic and lipid indices may be influenced by pharmacological therapy, dietary changes, and clinical monitoring, potentially reducing the observable differences between adiposity groups at a single time point. However, adipose tissue dysfunction may persist despite apparent similarities in HbA1c or lipid profiles. Obesity-related adipose tissue dysfunction is characterized by adipocyte hypertrophy, impaired lipid storage capacity, altered adipokine secretion, inflammatory remodeling, and vascular dysfunction [33, 34]. Therefore, the observed adipokine pattern may represent an endocrine signal of adipose tissue stress that is not captured by standard laboratory parameters.

Adiponectin showed a significant reduction in obese participants compared with overweight participants. This finding is consistent with the established role of adiponectin as an insulin-sensitizing, anti-inflammatory, and vasculoprotective protein. Lower adiponectin concentrations are commonly associated with obesity, impaired adipose tissue function and increased cardiometabolic risk. However, adiponectin biology is complex, and paradoxical associations have been described in selected clinical populations, particularly in relation to cardiovascular outcomes and mortality [35]. In the present study, lower adiponectin levels in obesity likely reflect impaired adipose endocrine function rather than a direct measure of insulin resistance, because fasting insulin and HOMA-IR were not assessed.

A notable finding was the significant BMI category × sex interaction for adiponectin, with obese females showing lower adiponectin concentrations than obese males, whereas overweight males and females had comparable values. This suggests that the obesity-associated reduction in adiponectin levels may differ by sex. Such a pattern is biologically plausible because adipose tissue distribution, adipocyte expandability, sex

hormone signalling, and metabolic flexibility differ between men and women [36–38]. Nevertheless, this result must be interpreted cautiously because the obese female subgroup was small. Therefore, adiponectin interactions should be considered hypothesis-generating rather than confirmatory. Larger sex-balanced studies are required to determine whether this pattern is reproducible and has clinical or prognostic significance.

FABP4 showed one of the clearest obesity-associated increases in this study cohort. FABP4 is an adipocyte- and macrophage-derived lipid-binding protein involved in fatty acid trafficking, inflammation of adipose tissue, and metabolic regulation. Elevated FABP4 concentrations have been linked to obesity, insulin resistance, diabetes, and cardiometabolic risks [39–41]. In the present study, FABP4 levels were significantly higher in obese participants of both sexes, with no significant BMI category × sex interaction. This suggests that FABP4 may primarily reflect adiposity-related adipose tissue stress rather than a sex-specific effect in this sample population. The consistency of FABP4 elevation across the male and female subgroups supports its potential value as part of a broader adipokine profile characterizing obesity-related metabolic dysfunction in T2DM.

RBP4 concentrations were significantly higher in obese participants. RBP4 has been implicated in obesity-related metabolic dysregulation through its relationship with adipose tissue function, hepatic metabolism, lipid handling and impaired insulin signalling [42–44]. The present findings support the concept that RBP4 may be an adipose-hepatic marker of obesity-associated metabolic stress. Importantly, RBP4 levels were elevated despite comparable glycemic indices between overweight and obese participants, suggesting that RBP4 may provide information beyond HbA1c or glucose measurements in clinically managed T2DM. However, because this study was cross-sectional, the findings cannot establish whether increased RBP4 contributes to metabolic deterioration or merely reflects the underlying adipose tissue dysfunction.

Visfatin concentrations were significantly higher in obese participants than in overweight ones. Visfatin has been associated with obesity-related inflammatory and metabolic pathways, although its interpretation remains less consistent than that of adiponectin and FABP4 [45, 46]. In this study, visfatin levels were elevated in both male and female obese participants, with no significant sex interaction. This supports the interpretation that visfatin may act as part of a broader obesity-associated inflammatory metabolic adipokine pattern rather than as an isolated diagnostic marker. Given the heterogeneity of visfatin findings in the previous literature, its greatest value may lie in combined adipokine profiling rather than independent interpretation.

Taken together, these findings indicate a coordinated obesity-associated endocrine shift in adults with T2DM. The pattern of elevated RBP4, FABP4, and visfatin levels, together with reduced adiponectin levels, is consistent with impaired adipose tissue function and inflammatory-metabolic remodeling. This shift was observed even though routine glycemic and lipid markers were similar between the groups. These results support the possibility that adipokine profiling may help characterize metabolic heterogeneity among individuals with T2DM, particularly in relation to obesity-related adipose tissue dysfunction. However, the present study did not establish diagnostic, prognostic, or therapeutic utility, and the findings should therefore be interpreted as biologically informative rather than immediately clinically actionable.

The present results also highlight the limitations of relying exclusively on BMI and routine biochemical indices to characterize obesity-related metabolic risk. BMI is useful for classifying adiposity status but does not directly measure visceral fat, ectopic lipid deposition, or adipose tissue quality. Similarly, HbA1c and lipid parameters provide important clinical information but may not reflect the endocrine and inflammatory states of adipose tissue. Recent studies have emphasized the potential value of visceral adiposity-related indices and metabolic risk markers in identifying diabetes and prediabetes risk in diverse populations [47, 48]. In this context, adipokines may complement conventional markers by providing additional insights into adipose tissue dysfunction. Future studies incorporating validated visceral adiposity indices or direct imaging-based measures of visceral fat would help clarify the relationship between adipokines, fat distribution, and metabolic risk in patients with T2DM.

The sex-stratified component of this study adds an important exploratory dimension to the existing literature. Although RBP4, FABP4, and visfatin showed broadly similar obesity-associated increases in men and women, adiponectin appeared to demonstrate a sex-dependent pattern. This may reflect differences in adipose tissue distribution, hormonal regulation, and adipocyte function. However, because the obese female subgroup included only nine participants, this finding should not be overinterpreted. Instead, it should be used to generate a testable hypothesis for future studies with adequate female representation, assessment of menopausal status, and adjustment for relevant hormonal and treatment-related variables.

This study had several strengths. First, it assessed multiple adipokines simultaneously within the same T2DM cohort, allowing the evaluation of a broader adipose endocrine profile rather than a single biomarker. Second, the inclusion of both overweight and obese participants enabled comparisons across clinically relevant adiposity categories. Third, the sex-stratified analysis allowed for the preliminary exploration of whether obesity-associated adipokine patterns differed between males and females. Fourth, this study included routine glycemic, lipid, renal, hepatic, and anthropometric parameters, providing a clinical context for interpreting adipokine differences.

This study also had some important limitations. The cross-sectional design of this study prevents conclusions regarding causality, temporality, or prediction of future cardiometabolic outcomes. The sample size was modest, and the obese female subgroup was small, limiting the statistical power for interaction analyses. Therefore, the observed adiponectin interactions should be regarded as exploratory. The study did not include normal-weight individuals with T2DM or non-diabetic controls, which limits the interpretation of whether the observed adipokine patterns are specific to obesity severity within T2DM or reflect broader diabetes-related changes. BMI and waist circumference were used as adiposity measures; however, direct imaging-based quantification of visceral or ectopic fat was not performed. In addition, fasting insulin and HOMA-IR levels were not measured; therefore, insulin resistance could not be directly evaluated. Information on diabetes duration, menopausal status, smoking, physical activity, dietary intake, and medication use was not incorporated into the present analysis, and these factors may have influenced adipokine concentrations. Finally, although ELISA procedures were performed according to the manufacturer’s instructions with duplicate analysis and quality control procedures, preanalytical and assay-related variability cannot be completely excluded.

Overall, the present findings indicate that obesity in adults with T2DM is associated with coordinated alterations in circulating adipokines, even when routine glycemic and lipid indices are comparable. This pattern supports the concept that adipokine profiling may provide additional biological insights into obesity-related adipose tissue dysfunction beyond conventional clinical markers. However, given the cross-sectional design and small obese female subgroup, the sex-related adiponectin findings should be interpreted as exploratory and require confirmation in larger, sex-balanced cohorts.

5. Conclusion

In adults with T2DM, obesity was associated with a distinct circulating adipokine profile characterized by elevated RBP4, FABP4, and visfatin levels and reduced adiponectin levels. These alterations were observed despite broadly comparable glycemic and lipid parameters, suggesting that adipokines may reflect obesity-related adipose tissue dysfunction not captured by routine metabolic markers. The observed BMI category × sex interaction for adiponectin is hypothesis-generating and should be confirmed in larger, sex-balanced longitudinal studies incorporating direct or validated surrogate measures of visceral adiposity, insulin resistance, treatment exposure, and relevant sex-specific clinical variables.

Abbreviations

A/G
albumin-to-globulin ratio
ALT
alanine aminotransferase
AST
aspartate aminotransferase
BMI
body mass index
BP
blood pressure
ELISA
enzyme-linked immunosorbent assay
FABP4
fatty acid-binding protein 4
HbA1c
glycated hemoglobin
HDL
high-density lipoprotein
HOMA-IR
homeostatic model assessment of insulin resistance
LDL
low-density lipoprotein
RBP4

retinol-binding protein 4
SD
standard deviation
TC
total cholesterol
T2DM
type 2 diabetes mellitus
VLDL
very low-density lipoprotein

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Board of Gulf Medical University, Ajman, United Arab Emirates (Approval No. IRB/COM/FAC/05/2018). Written informed consent was obtained from all participants before enrolment. All study procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki and its subsequent amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no external funding.

Author Contribution

AS performed investigation, data curation, formal analysis, project administration, and drafted the original manuscript. MJ supervised the study and contributed to clinical interpretation. PM contributed to conceptualization and methodology. AK supervised the study and contributed to scientific interpretation. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions protecting participant confidentiality.

References

1. Worldwide trends in diabetes prevalence and treatment. from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. Lancet. 2024;404(10467):2077–93. https://doi.org/10.1016/S0140-6736(24)02317-1.
2. Chandrasekaran P, Weiskirchen R. The Role of Obesity in Type 2 Diabetes Mellitus-An Overview. Int J Mol Sci. 2024;25(3):1882. https://doi.org/10.3390/ijms25031882.
3. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents and adults. Lancet. 2024;403(10431):1027–50. https://doi.org/10.1016/S0140-6736(23)02750-2.
4. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2025. Diabetes Care. 2025;48(1 Suppl 1):S27–49. https://doi.org/10.2337/dc25-S002.
5. Rubino F, Cummings DE, Eckel RH, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol. 2025;13(3):221–62. https://doi.org/10.1016/S2213-8587(24)00316-4.
6. Wu RL, Chen N, Chen Y, Wu X, Ko CY, Chen XY. Visceral Adiposity as an Independent Risk Factor for Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus: A Retrospective Study. J Diabetes Res. 2024;2024:9912907. https://doi.org/10.1155/2024/9912907.
7. Jakubiak GK, Badicu G, Surma S, Waluga-Kozłowska E, Chwalba A, Pawlas N. The Visceral Adiposity Index and Its Usefulness in the Prediction of Cardiometabolic Disorders. Nutrients. 2025;17(14):2374. https://doi.org/10.3390/nu17142374.
8. Shen F, Guo C, Zhang D, Liu Y, Zhang P. Visceral adiposity index as a predictor of type 2 diabetes mellitus risk: A systematic review and dose-response meta-analysis. Nutr Metab Cardiovasc Dis. 2024;34(4):811–22. https://doi.org/10.1016/j.numecd.2023.04.009.
9. Zhang Y, Gao W, Li B, et al. The association between the visceral obesity indices and the future diabetes mellitus risk: A prospective cohort study. Diabetes Obes Metab. 2025;27(8):4490–8. https://doi.org/10.1111/dom.16492.
10. Zhou H, Li T, Li J, Zhuang X, Yang J. The association between visceral adiposity index and risk of type 2 diabetes mellitus. Sci Rep. 2024;14(1):16634. https://doi.org/10.1038/s41598-024-67430-x.
11. An SM, Cho SH, Yoon JC. Adipose Tissue and Metabolic Health. Diabetes Metab J. 2023;47(5):595–611. https://doi.org/10.4093/dmj.2023.0011.
12. Bays HE, Bindlish S, Clayton TL. Obesity, diabetes mellitus and cardiometabolic risk: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2023. Obes Pillars. 2023;5:100056. https://doi.org/10.1016/j.obpill.2023.100056.

13. Reilly SM, Saltiel AR. Adapting to obesity with adipose tissue inflammation. Nat Rev Endocrinol. 2017;13(11):633–43. https://doi.org/10.1038/nrendo.2017.90.
14. Malicka A, Ali A, MacCannell ADV, Roberts LD. Brown and beige adipose tissue-derived metabokine and lipokine inter-organ signalling in health and disease. Exp Physiol. 2025;110(7):918–35. https://doi.org/10.1113/EP092008.
15. Czech MP. Mechanisms of insulin resistance related to white, beige and brown adipocytes. Mol Metab. 2020;34:27–42. https://doi.org/10.1016/j.molmet.2019.12.014.
16. Link JC, Reue K. Genetic Basis for Sex Differences in Obesity and Lipid Metabolism. Annu Rev Nutr. 2017;37:225–45. https://doi.org/10.1146/annurev-nutr-071816-064827.
17. Kvandova M, Puzserova A, Balis P. Sexual Dimorphism in Cardiometabolic Diseases: The Role of AMPK. Int J Mol Sci. 2023;24(15):11986. https://doi.org/10.3390/ijms241511986.
18. Valencak TG, Osterrieder A, Schulz TJ. Sex matters: The effects of biological sex on adipose tissue biology and energy metabolism. Redox Biol. 2017;12:806–13. https://doi.org/10.1016/j.redox.2017.04.012.
19. Mauvais-Jarvis F. Sex differences in metabolic homeostasis, diabetes and obesity. Biol Sex Differ. 2015;6:14. https://doi.org/10.1186/s13293-015-0033-y.
20. Tramunt B, Smati S, Grandgeorge N, et al. Sex differences in metabolic regulation and diabetes susceptibility. Diabetologia. 2020;63(3):453–61. https://doi.org/10.1007/s00125-019-05040-3.
21. Deng R, Chen W, Zhang Z, et al. Association Between Visceral Obesity Index and Diabetes: A Systematic Review and Meta-analysis. J Clin Endocrinol Metab. 2024;109(10):2692–707. https://doi.org/10.1210/clinem/dgae303.
22. Vijayakumar S, Pantha S, Budha Magar S, Dhakal S. Sex Differences in the Impact of Obesity on Immunity. Immunol Rev. 2026;338(1):e70101. https://doi.org/10.1111/imr.70101.
23. Liu L, Shi Z, Ji X, et al. Adipokines, adiposity and atherosclerosis. Cell Mol Life Sci. 2022;79(5):272. https://doi.org/10.1007/s00018-022-04286-2.
24. Kim J, Oh CM, Kim H. The Interplay of Adipokines and Pancreatic Beta Cells in Metabolic Regulation and Diabetes. Biomedicines. 2023;11(9):2589. https://doi.org/10.3390/biomedicines11092589.
25. Francischetti EA, Dezonne RS, Pereira CM, et al. Insights Into the Controversial Aspects of Adiponectin in Cardiometabolic Disorders. Horm Metab Res. 2020;52(10):695–707. https://doi.org/10.1055/a-1239-4349.
26. Khan H, Parmar V, Khan MM, Khan S, Alam R. Role of the Genetic Variants of Fetuin-A and Adiponectin in Type 2 Diabetes Mellitus: A Narrative Review. Cureus. 2025;17(11):e95914. https://doi.org/10.7759/cureus.95914.
27. Han Y, Sun Q, Chen W, et al. New advances of adiponectin in regulating obesity and related metabolic syndromes. J Pharm Anal. 2024;14(5):100913. https://doi.org/10.1016/j.jpha.2023.12.003.
28. Huang J, Chen Y, Wang X, Wang C, Yang J, Guan B. Change in Adipokines and Gastrointestinal Hormones After Bariatric Surgery: a Meta-analysis. Obes Surg. 2023;33(3):789–806. https://doi.org/10.1007/s11695-022-06444-8.

29. Christou GA, Tselepis AD, Kiortsis DN. The metabolic role of retinol binding protein 4: an update. Horm Metab Res. 2012;44(1):6–14. https://doi.org/10.1055/s-0031-1295491.
30. Furuhashi M. Fatty Acid-Binding Protein 4 in Cardiovascular and Metabolic Diseases. J Atheroscler Thromb. 2019;26(3):216–32. https://doi.org/10.5551/jat.48710.
31. Dakroub A, A Nasser S, Younis N, et al. Visfatin: A Possible Role in Cardiovasculo-Metabolic Disorders. Cells. 2020;9(11):2444. https://doi.org/10.3390/cells9112444.
32. Lei X, Qiu S, Yang G, Wu Q. Adiponectin and metabolic cardiovascular diseases: Therapeutic opportunities and challenges. Genes Dis. 2022;10(4):1525–36. https://doi.org/10.1016/j.gendis.2022.10.018.
33. Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. Am J Physiol Cell Physiol. 2021;320(3):C375–91. https://doi.org/10.1152/ajpcell.00379.2020.
34. Koenen M, Hill MA, Cohen P, Sowers JR, Obesity. Adipose Tissue and Vascular Dysfunction. Circ Res. 2021;128(7):951–68. https://doi.org/10.1161/CIRCRESAHA.121.318093.
35. Menzaghi C, Trischitta V. The Adiponectin Paradox for All-Cause and Cardiovascular Mortality. Diabetes. 2018;67(1):12–22. https://doi.org/10.2337/dbi17-0016.
36. Pavlović N, Todorović P, Maglica M, Kumrić M, Božić J. Nutrient-Induced Remodeling of the Adipose-Cardiac Axis: Metabolic Flexibility, Adipokine Signaling and Therapeutic Implications for Cardiometabolic Disease. Nutrients. 2025;17(24):3945. https://doi.org/10.3390/nu17243945.
37. Mauvais-Jarvis F. Gender differences in glucose homeostasis and diabetes. Physiol Behav. 2018;187:20–3. https://doi.org/10.1016/j.physbeh.2017.08.016.
38. Gavin KM, Bessesen DH. Sex Differences in Adipose Tissue Function. Endocrinol Metab Clin North Am. 2020;49(2):215–28. https://doi.org/10.1016/j.ecl.2020.02.008.
39. Van der Ark-Vonk EM, Puijk MV, Pasterkamp G, van der Laan SW. The Effects of FABP4 on Cardiovascular Disease in the Aging Population. Curr Atheroscler Rep. 2024;26(5):163–75. https://doi.org/10.1007/s11883-024-01196-5.
40. Trojnar M, Patro-Małysza J, Kimber-Trojnar Ż, Leszczyńska-Gorzelak B, Mosiewicz J. Associations between Fatty Acid-Binding Protein 4-A Proinflammatory Adipokine and Insulin Resistance, Gestational and Type 2 Diabetes Mellitus. Cells. 2019;8(3):227. https://doi.org/10.3390/cells8030227.
41. Parra S, Cabré A, Marimon F, et al. Circulating FABP4 is a marker of metabolic and cardiovascular risk in SLE patients. Lupus. 2014;23(3):245–54. https://doi.org/10.1177/0961203313517405.
42. Nono Nankam PA, Blüher M. Retinol-binding protein 4 in obesity and metabolic dysfunctions. Mol Cell Endocrinol. 2021;531:111312. https://doi.org/10.1016/j.mce.2021.111312.
43. Fan J, Hu J. Retinol binding protein 4 and type 2 diabetes: from insulin resistance to pancreatic β-cell function. Endocrine. 2024;85(3):1020–34. https://doi.org/10.1007/s12020-024-03777-5.
44. Schiborn C, Weber D, Grune T, et al. Retinol and Retinol Binding Protein 4 Levels and Cardiometabolic Disease Risk. Circ Res. 2022;131(7):637–49. https://doi.org/10.1161/CIRCRESAHA.122.321295.
45. Abdalla MMI. Role of visfatin in obesity-induced insulin resistance. World J Clin Cases. 2022;10(30):10840–51. https://doi.org/10.12998/wjcc.v10.i30.10840.

46. Yilmaz DT, Gul MA, Capraz M, Demir HD, Tekcan A. Investigation of Serum Visfatin and Chemerin Levels in Type 2 Diabetes and Obesity Patients: Their Potential Role as Clinical and Biomarkers. Biomedicines. 2025;13(11):2619. https://doi.org/10.3390/biomedicines13112619.
47. Zheng D, Zhao C, Ma K, et al. Association between visceral adiposity index and risk of diabetes and prediabetes: Results from the NHANES (1999–2018). PLoS ONE. 2024;19(4):e0299285. https://doi.org/10.1371/journal.pone.0299285.
48. Lv C, Huo R. Association between visceral adiposity index, lipid accumulation product and type 2 diabetes mellitus in US adults with hypertension: a cross-sectional analysis of NHANES from 2005 to 2018. BMC Endocr Disord. 2024;24(1):216. https://doi.org/10.1186/s12902-024-01750-x.

Figures

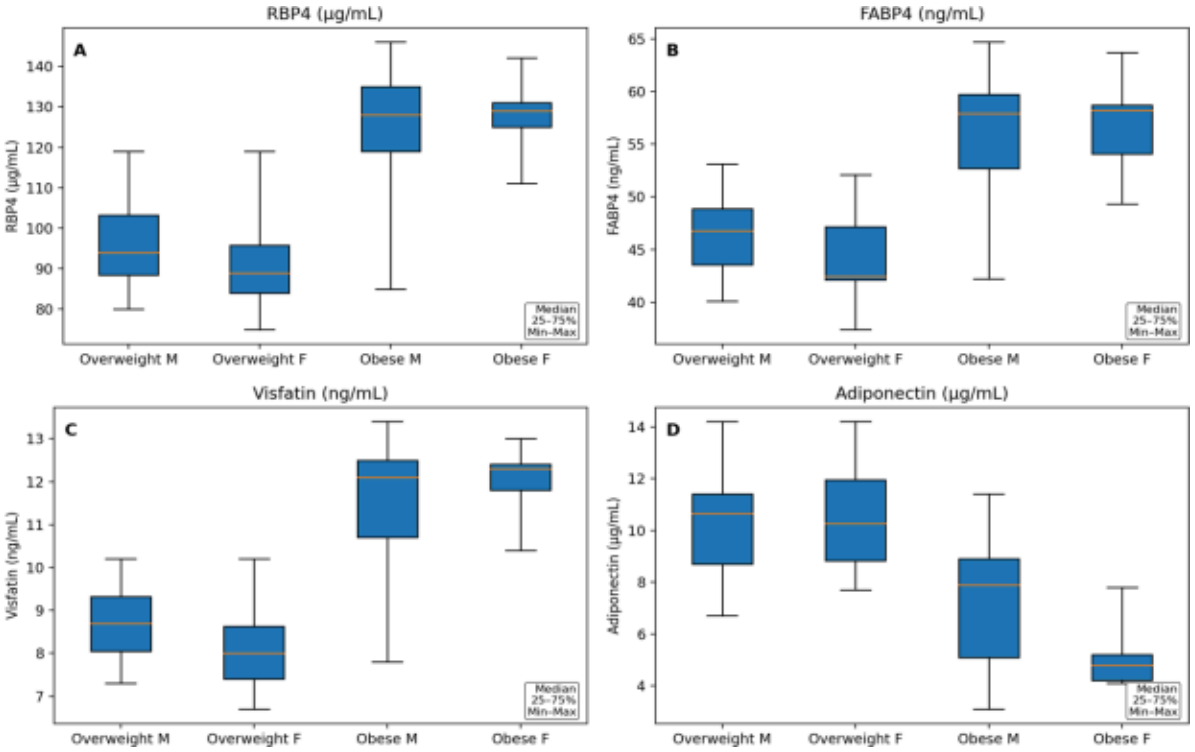


Figure 1

Demonstrates that the obesity-associated differences are not confined to mean shifts but reflect consistent distribution-level changes in medians, interquartile ranges, and overall ranges across subgroups.

Figure 1A (RBP4): Both obese males and females showed an upward shift relative to overweight males and females, with higher medians and overall distributions. The separation between the overweight and obese strata was visually clear, supporting RBP4 as a robust discriminator of obesity status in T2DM. The male and female distributions within each BMI category were broadly similar, consistent with the lack of a strong BMI category × gender interaction.

Figure 1B (FABP4): FABP4 displayed one of the most pronounced separations between the overweight and obese strata, with higher medians and upward-shifted interquartile ranges in both obese subgroups. The

relatively tight clustering within groups (narrower IQRs) and a large between-category shift suggest a strong and consistent obesity-associated effect. Sex differences were modest within BMI categories, reinforcing that the main driver was the BMI category rather than sex.

Figure 1C (visfatin): Visfatin distributions shifted upward with obesity in both males and females, with obese strata showing higher medians and higher overall ranges than the overweight strata. Compared with FABP4, visfatin showed a slightly greater within-group spread; however, the between-category separation remained substantial, supporting a strong association between obesity and visfatin elevation in T2DM.

Figure 1D (Adiponectin): Adiponectin showed the reverse direction, with the obese strata shifted downward compared with the overweight strata, consistent with the suppression of a protective insulin-sensitizing adipokine in obesity. Importantly, Figure 1D visually supports the BMI category × sex interaction: overweight males and females have overlapping adiponectin distributions, whereas obese females show a noticeably lower distribution than obese males (lower median and lower IQR), consistent with a steeper obesity-associated decline among females in this cohort. Given the smaller obese female subgroup (n=9), this finding is best interpreted as statistically supported but requiring cautious generalization.