Clinical Research

Association between high serum levels of soluble vascular cell adhesion molecule-1 and obesity in women

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ABSTRACT

BACKGROUND Obesity and metabolic disorders are associated with persistent low-level inflammation connected to soluble vascular cell adhesion molecule-1 (sVCAM-1). Recent research highlights its connection to endothelial dysfunction in female obesity. This study aimed to investigate the relationship between sVCAM-1 levels and obesity-related risk factors in women from Kirkuk City, Iraq.

METHODS A case-control study was conducted on 90 women aged 20–50, including 43 participants with obesity and 47 healthy controls. Blood samples were collected, processed, and analyzed to measure various biochemical markers, including sVCAM-1. Logistic regression analysis was utilized to examine the association between sVCAM-1 levels and obesity-related parameters. Correlation analysis was performed to assess associations with body mass index (BMI). Statistical analysis was conducted using SPSS software version 23.0.

RESULTS Correlation analysis revealed that BMI was significantly correlated with alanine aminotransferase ($r = 0.37$, $p = 0.011$), uric acid ($r = 0.30$, $p = 0.04$), insulin ($r = 0.37$, $p = 0.01$), homeostatic model assessment of insulin resistance ($r = 0.47$, $p = 0.002$), and sVCAM-1 ($r = 0.53$, $p = 0.001$). These results suggest that elevated sVCAM-1 levels may serve as predictive biomarkers for increased insulin resistance in obese individuals. These findings indicate that sVCAM-1 is strongly linked to female obesity and insulin resistance.

CONCLUSIONS This study confirms the potential use of sVCAM-1 as a prognostic biomarker for obesity-related metabolic disturbances and its role in identifying individuals with a higher risk of developing insulin resistance.

KEYWORDS adhesion molecule-1, body mass index, homeostatic model assessment, obesity, vascular cell

A body mass index (BMI) exceeding 30 kg/m² is classified as obese, a condition increasingly prevalent in both high- and low-income countries. Currently, an estimated 1.9 billion people worldwide are overweight or obese, and this number is projected to reach 58% of the global population by 2030.[1] Obesity is primarily characterized by excess adipose tissue, which produces pro-inflammatory cytokines that can contribute to metabolic disorders.[1–4]

Compared to individuals with normal BMIs, individuals with obesity exhibit higher levels of these pro-inflammatory cytokines, which have been linked to various metabolic conditions.[5] Additionally, they show elevated levels of soluble vascular cell adhesion molecule-1 (sVCAM-1), a recognized marker of inflammation and endothelial activation.[6,7] sVCAM-1 facilitates leukocyte adherence to endothelial cells (ECs) and is considered a potential biomarker for

atherosclerosis, metabolic dysfunctions like insulin resistance and dyslipidemia, and cardiovascular disorders.[8,9]

Recent research indicates a link between elevated sVCAM-1 levels and obesity-related metabolic abnormalities, including BMI and other metabolic markers.[9] Pro-inflammatory cytokines and other substances secreted from adipose tissue are thought to influence sVCAM-1 expression, with higher levels observed in individuals with increased abdominal fat.[10] Therefore, this study aimed to understand the correlation between serum sVCAM-1 levels and obesity in women by comparing women who are obese with women who are of normal weight and analyzing its association with BMI, anthropometric, and biochemical factors.

METHODS

Ethics statement

The study was approved by the Research Ethics Committee at the College of Pharmacy, University of Kirkuk between April and August 2023 (Ref. No: 7/27/3267) following the Declaration of Helsinki. The study was subsequently conducted at the Ashit Central Advanced Laboratory in Kirkuk Province, Iraq.

Study population

A random sampling method was used to select participants, with the sample size determined using a sample size calculator (Raosoft Inc, USA).[11] For a 95% confidence level and a 5% margin of error, a minimum sample size of 74 was deemed appropriate. A total of 90 women aged 20–50 from Kirkuk City were recruited. Matching was performed between cases and controls, comprising 43 individuals with obesity and 47 healthy controls. Exclusion criteria included a diagnosis of diabetes, hypertension, hepatic pathology, endocrine disorders, cardiac or renal impairment, or cancer. Smokers and those who had ingested alcohol were also excluded. Participants in the obese group required an average BMI of 34.86 (0.55) kg/m^2. According to the World Health Organization classification, BMI ranges are defined as follows: normal weight (18.5–24.9 kg/m^2), obese (30–39.9 kg/m^2), and morbidly obese (≥40 kg/m^2).[12]

Sociodemographic data, including age, marital status, residence, educational attainment, and physical activity level, were obtained using a questionnaire. Physical activity was evaluated using a condensed form of the International Physical Activity Questionnaire, which contains seven criteria that classify participants into high, moderate, and low activity levels based on the frequency (days) and duration (minutes and/or hours) of intense, moderately intense, walking, and seated activities.

Biochemical assays

For laboratory analysis, 5 mL of venous blood was collected from each participant after an overnight fast.[13] The samples were centrifuged at 30,000 × *g* for 15 min for serum separation. The separated serum was then transferred to Eppendorf tubes and stored at –20 °C until further analysis. Fasting blood glucose (FBG) levels were measured using a RANSEL RS 505 kit (Randox Laboratories, UK). This method employs enzymatic oxidation by glucose oxidase, which yields hydrogen peroxide. The hydrogen peroxide then reacts with phenol and 4-aminophenazone in the presence of peroxidase to produce a pink hue, with its intensity correlating with the glucose concentration in the blood serum.[14,15] An enzyme-linked immunosorbent assay (ELISA) kit (Elabscience, China) was used to determine insulin titers. The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the formula: (insulin × glucose)/22.5.[16,17]

Lipid profiles, including total cholesterol, triglyceride, and low-density lipoprotein concentrations, were analyzed using KENZA 450 TX (BIOLABO, Japan). Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were measured using Randox kits (Randox Laboratories Ltd., UK) and bioMérieux kits (bioMérieux, France), respectively. Urea titers were derived from the Erba kit assay (Urea UV Auto; Erba Lachema s.r.o, Czech Republic), based on absorbance correlation over time. Serum uric acid was quantified using the BioAssay Uric Acid Test Kit (BioAssay Systems, USA), where the blue chemical 2,4,6-tripyridyl-s-triazine was combined with iron upon uric acid detection. The resulting color intensity was measured at a wavelength of 590 nm. Serum creatinine was quantified using a Serum Creatinine kit (DetectX®; Arbor Assays, USA), with the color intensity measured at 490 nm after 60 s using a microtiter plate reader (Molecular Devices, USA). Human sVCAM-1 levels were also measured using the same ELISA kit (Elabscience).

Statistical analysis

Data was analyzed using SPSS software version 23.0 (IBM Corp., USA). The Kolmogorov–Smirnov test was used to confirm the normality of each continuous variable. Categorical variables were presented as frequencies and proportions. Fischer's exact test was applied when more than 20% of cells had expected counts less than 5, and Pearson's chi-squared test was used otherwise. The students' *t*-test was used for continuous data comparisons, with the results presented as mean (standard error [SE]). Logistic regression analysis was employed to evaluate the relationship between risk factors and obesity, while Pearson's correlation coefficient was used to assess the associations between variables. Statistical significance was set at $p<0.05$.

RESULTS

Sociodemographic data are presented in Table 1. The prevalence of obesity increased with age, particularly among individuals aged 41–50 years (60%), and varied according to marital status and educational level. Obesity was significantly more common among married participants (70%) and those with secondary education (56%), whereas no significant differences were observed based on residency or physical activity level.

Table 2 compares various variables between the obese and control groups. BMI, FBG, insulin, HOMA-IR, and sVCAM-1 levels differed significantly between the groups ($p = 0.001$). Participants with obesity showed elevated BMI, FBG, insulin, HOMA-IR, and sVCAM-1 levels compared to controls. Table 3 presents the results of the univariate regression analysis examining the relationship between risk factors and obesity. Multiple regression analysis further indicated that sVCAM-1 levels were approximately three times higher in participants with obesity than in those with normal weight (odds ratio [OR]: 2.97; 95% confidence interval [CI]: 1.41–5.01). Table 4 displays the results of the correlation analysis, revealing a strong positive correlation between BMI and FBG, insulin, HOMA-IR, ALT, serum uric acid, and sVCAM-1 levels.

Table 1. Sociodemographic characteristics of studied populations

Variables	Groups, n (%)		*p*
	Obese (N = 43)	Control (N = 47)	
Age (years)			**0.001**
20–30	11 (26)	10 (21)	
31–40	6 (14)	23 (49)	
41–50	26 (60)	14 (30)	
Marital status			**0.001**
Single	10 (23)	29 (62)	
Married	30 (70)	14 (30)	
Divorced/widowed	3 (7)	4 (9)	
Place of residence			0.572
Rural	7 (16)	8 (17)	
Urban	36 (84)	39 (83)	
Educational level			**0.003**
Primary education	11 (26)	14 (30)	
Secondary education	24 (56)	11 (23)	
Higher education	8 (19)	22 (47)	
Physical activity level			0.474
Low	13 (30)	9 (19)	
Moderate	27 (63)	33 (70)	
High	3 (7)	5 (11)	

Table 2. Comparison of various variables between the obese and normal groups

Variables	Groups, LSM (SE)		*p*
	Obese (N = 43)	Control (N = 47)	
Age (years)	41.88 (0.82)	34.82 (0.83)	0.322
BMI (kg/m^2)	34.86 (0.55)	22.71 (0.23)	**0.001**
FBG (mmol/l)	6.79 (0.11)	4.28 (0.06)	**0.001**
Insulin (ng/ml)	40.92 (2.16)	23.83 (1.24)	**0.001**
HOMA-IR	8.79 (0.53)	4.48 (0.23)	**0.001**
Total cholesterol (mmol/l)	5.33 (0.11)	4.20 (0.09)	0.913
Triglyceride (mmol/l)	1.44 (0.04)	1.00 (0.05)	0.210
LDL cholesterol (mmol/l)	2.84 (0.06)	2.49 (0.05)	0.894
ALT (U/l)	16.81 (1.04)	14.00 (0.98)	0.707
AST (U/l)	21.51 (1.10)	19.57 (1.02)	0.755
Serum urea (mmol/l)	5.09 (0.13)	4.89 (0.11)	0.226
Serum uric acid (mg/dl)	4.91 (0.18)	4.41 (0.14)	0.113
Serum creatinine (mg/dl)	0.57 (0.06)	0.62 (0.05)	0.725
sVCAM-1 (ng/ml)	43.58 (5.25)	25.17 (2.62)	**0.001**

ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; FBG=fasting blood glucose; HOMA-IR=homeostatic model assessment of insulin resistance; LDL=low-density lipoprotein; LSM=least square means; SE=standard error; sVCAM-1=soluble vascular cell adhesion molecule-1

Table 3. Logistic regression analysis of risk factors associated with obesity

Variables	Univariate logistic regression			Multivariate logistic regression		
	Estimate	OR (95% CI)	*p*	Estimate	OR (95% CI)	*p*
Age (years)	0.04	1.04 (0.89–3.62)	0.288	-	-	-
FBG (mmol/l)	0.15	1.16 (1.02–4.17)	**0.030**	0.31	1.13 (1.04–3.26)	0.309
Insulin (ng/ml)	0.26	1.29 (0.84–3.10)	**0.025**	0.20	1.22 (1.01–3.56)	0.258
HOMA-IR	0.33	1.39 (0.97–3.44)	**0.030**	0.14	1.15 (0.94–2.90)	0.185
Total cholesterol (mmol/l)	0.10	1.10 (0.91–3.76)	0.364	-	-	-
Triglyceride (mmol/l)	0.09	1.09 (0.80–3.16)	0.625	-	-	-
LDL cholesterol (mmol/l)	0.21	1.23 (0.90–4.15)	0.547	-	-	-
ALT (U/l)	0.11	1.11 (1.00–3.30)	0.357	-	-	-
AST (U/l)	0.07	1.07 (0.81–3.16)	0.406	-	-	-
Serum urea (mmol/l)	0.16	1.17 (0.98–3.14)	0.130	-	-	-
Serum uric acid (mg/dl)	0.06	1.06 (0.96–3.10)	0.247	-	-	-
Serum creatinine (mg/dl)	0.24	1.27 (1.06–4.23)	0.440	-	-	-
sVCAM-1(ng/ml)	0.99	2.69 (1.11–5.08)	**0.001**	1.09	2.97 (1.41–5.01)	**0.002**

ALT=alanine aminotransferase; AST=aspartate aminotransferase; CI=confidence interval; FBG=fasting blood glucose; HOMA-IR=homeostatic model assessment of insulin resistance; LDL=low-density lipoprotein; OR=odds ratio; sVCAM-1=soluble vascular cell adhesion molecule-1

Table 4. Correlation coefficients for BMI versus the concentrations of various parameters in obese women

Variables	BMI (kg/m^2)	
	r	*p*
Age (years)	0.17	0.264
FBG (mmol/l)	0.36	**0.012**
Insulin (ng/ml)	0.37	**0.010**
HOMA-IR	0.47	**0.002**
Total cholesterol (mmol/l)	0.06	0.665
Triglyceride (mmol/l)	0.10	0.494
LDL cholesterol (mmol/l)	0.22	0.145
ALT (U/l)	0.37	**0.011**
AST (U/l)	0.01	0.926
Serum urea (mmol/l)	0.25	0.109
Serum uric acid (mg/dl)	0.30	**0.040**
Serum creatinine (mg/dl)	0.22	0.156
sVCAM (ng/ml)	0.53	0.001

ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; FBG=fasting blood glucose; LDL=low-density lipoprotein; r=correlation coefficient; HOMA-IR=homeostatic model assessment of insulin resistance; sVCAM-1=soluble vascular cell adhesion molecule-1

DISCUSSION

Obesity, a global issue affecting both high- and low-income countries, is characterized by excessive adipose tissue. This is reflected in increased BMI and insulin resistance, leading to hyperglycemia and inflammation.[3,18–21] Dysfunctional adipose tissue releases pro-inflammatory adipokines, which impair insulin signaling pathways in target organs like the liver, muscles, and adipose tissue itself. Insulin-activated serine kinases phosphorylate insulin receptor substrates and disrupt signaling pathways. This reduces cellular glucose uptake and glycogen synthesis and increases hepatic glucose production and FBG values.[22]

Age was a key factor in the sociodemographic profiles of the participants, suggesting that obesity rates increase with age. This trend may be attributed to various metabolic changes in the body, including decreased basal metabolic rate, which promotes weight gain and increases obesity risk.[23] Additionally, hormonal changes, including reduced estrogen levels, affect fat distribution and potentially increase obesity risk in older women. A deficiency in vitamins or trace elements may further exacerbate metabolic dysfunction, causing susceptibility to obesity-related diseases, such as diabetes.[24–26] Educational level and marital status also showed significant correlations with obesity, consistent with previous research findings.[11,27]

Furthermore, obesity-induced lipolysis increases circulating free fatty acids, interfering with insulin signaling and worsening insulin resistance by causing alterations in peripheral tissues' glucose metabolism.[28,29] Hyperinsulinemia and inflammation

are key contributors to functional impairment of the endothelium; both are present in obesity and are linked to associated health issues.[30] Endothelium impairment triggers plaque formation, driving the progression of atheroma pathogenesis and resulting in an increased risk of cardiovascular events.[31] Obesity likely plays a significant role in this dysfunction.

Several mechanisms have been proposed to explain the association between obesity and endothelial dysfunction. Adipocytes synthesize inflammatory mediators, while metabolic elements, such as insulin levels, influence endothelial function, potentially through sVCAM-1.[32] Both obesity and insulin resistance are linked to endothelial dysfunction.[34] This challenge to homeostasis results in reduced nitric oxide bioavailability, leading to a dysfunctional vessel phenotype characterized by amplified cell adhesion molecule (CAM) expression, particularly of sVCAM-1.[33] This protein, found in ECs, smooth muscle cells, and macrophages, plays a key role in facilitating the interplay between different immune cells, such as the initial bonding and rolling of monocytes and lymphocytes. sVCAM-1 enables leukocyte adhesion and migration across the endothelial layer into the vascular wall.[34,35] Research consistently indicates elevated sVCAM-1 levels in patients with obesity and diabetes compared to those in controls.[36] Similarly, this study found higher sVCAM-1 levels in participants with obesity than in healthy controls.

Obesity is associated with elevated levels of bioindicators and CAMs, reflecting ongoing inflammation and the loss of vascular endothelial function. Consequently, vascular cell adhesion molecules may serve as a cardiovascular risk biomarker.[15,37] Excess adipose tissue secretes pro-inflammatory molecules that trigger an inflammatory response and activate ECs, which then express adhesion molecules, such as vascular cell adhesion molecule-1 (VCAM-1).[38] Additionally, obesity-related adipose accumulation is linked to inadequate blood vessel development, leading to hypoxia, which further induces the production of adhesion molecules and pro-inflammatory cytokines, including sVCAM-1.[39] Increased VCAM-1 expression promotes the adhesion of immune cells, such as monocytes and lymphocytes, to the ECs,[40,41] enhancing bonding between the endothelium and leukocytes and facilitating white blood cell migration into the perivascular compartment.[42] An evaluation of adhesion status can provide insights into the impact of environmental factors on vascular disease.[6]

Early detection of biomarkers after disease onset is crucial for managing conditions, such as diabetes, as measuring insulin resistance before clinical symptoms appear remains challenging.[43] Research indicates that early-life obesity is linked to greater BMI, insulin concentrations, HOMA-IR, lipid profiles, and sVCAM-1 titer.[38,44] This study also found significant associations between BMI in participants with obesity and FBG, insulin levels, HOMA-IR, ALT, serum uric acid, and sVCAM-1 titers, which is consistent with previous studies. Previous studies have also demonstrated a positive association between BMI and FBG ($r = 0.0751$, $p<0.0001$).[19] Pearson's correlation analysis showed that BMI is related to insulin, HOMA-IR, ALT, and uric acid levels in patients with obesity.[44–46] Increased soluble CAMs, such as sVCAM-1, are elevated in individuals who are obese and overweight and have a robust correlation with BMI.[47,48]

To our knowledge, this is the first study in Kirkuk Governorate to compare adhesion molecules between women who are obese with insulin resistance and normal weight controls. We also examined the relationships between sVCAM-1 levels and various anthropometric and biochemical markers. However, the study was limited by its small sample size and predominantly female participants, which may have affected the generalizability of the results. Further research is required to explore the temporal relationship between the changes in sVCAM-1 levels and the development of obesity-related complications. Long-term studies are necessary to investigate the potential correlation between sVCAM-1 and other markers of endothelial dysfunction in obesity.

In conclusion, our results from the Kirkuki population suggest that women with obesity exhibit increased endothelial dysfunction and heightened pro-inflammatory responses, as indicated by elevated sVCAM-1 levels and greater insulin resistance. These results support the potential use of sVCAM-1 as a biomarker for obesity-related metabolic disturbances. However, further studies are needed to confirm this hypothesis. Larger longitudinal studies are required to investigate the association between sVCAM-1 levels and obesity-related complications, particularly insulin resistance.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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