

# Study of Adhesion Molecules in Type 2 Diabetes Mellitus Iraqi Patients with Dyslipidemia

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## Abstract:

**Background:** Cell adhesion molecules are protein entities that are located on the cell surface. The vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) expression is related to type 2 diabetes mellitus (T2DM) with dyslipidemia.

**Objectives:** To determine the levels of VCAM-1 and ICAM-1 in T2DM patients with dyslipidemia and to explore the relationship between VCAM-1 and ICAM-1 and the development of dyslipidemia in T2DM patients.

**Methods:** The study included 150 individuals with an age range of (35-55) years. Patients with diabetes for more than 5 years were excluded. Fifty healthy individuals constituted Group 1 (G1), fifty patients with T2DM constituted Group 2 (G2), and fifty T2DM patients with dyslipidemia constituted Group 3 (G3). Whole blood samples were drawn to measure HbA1c based on fluorescence immunoassay technology. The serum was separated to measure fasting blood glucose (FBG), triglycerides (TG), total cholesterol (TC), and high-density lipoproteins (HDL) by manual methods, while VCAM-1, and ICAM-1 were determined using the ELISA test. The study was conducted between November 2022 and April 2023 at the National Center for Diabetes Treatment and Research, Baghdad, Iraq.

**Results:** Significantly higher levels of FSG and HbA1c were detected in G2 and G3 compared to G1, but non-significantly so when G3 was compared to G2. Significant higher levels of TG and TC levels were detected for G3 when compared to G1 and G2, but non-significantly so when G2 was compared to G1. HDL levels were significantly lower in G3 compared to G2 and G1, but non-significantly so when G2 was compared to G1. VCAM-1, and ICAM-1 were significantly higher in G2 compared to G1, and VCAM-1 level was significantly higher in G3 compared to G2. Non-significant differences in ICAM-1 levels were found between G3 and G2.

**Conclusion:** VCAM-1 and ICAM-1 are potentially significant factors in the development of dyslipidemia in diabetes patients. They might serve as biomarkers to accurately predict the progression of cardiovascular disease.

**Keywords:** Diabetes mellitus; Dyslipidemia; VCAM-1; ICAM-1.

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## Introduction:

The characteristic of diabetic dyslipidemia is hyperglycemia with lipoprotein abnormalities. Over 70% of those who have T2DM are affected by dyslipidemia making it a fairly common condition. Diabetes confers a greatly increased risk of cardiovascular disease (1,2). The VCAM-1 is a protein that also contains T-cell receptors and antibodies (3). Studies demonstrate relationships among the sVCAM-1 and sICAM in patients of T2DM with cardiovascular disease (CVD) and revealed that abnormalities in endothelium cause a rise in these markers (4,5). The ICAM-1 is a glycoprotein that is found in microglial cells, astrocytes, central nervous system in addition to endothelial cells (white and grey human forebrain) (6,7). Because of dyslipidemia, cholesterol builds up and becomes oxidized, which speeds up the activation of ICAM-1 for monocyte adhesion. This causes a rise

in the number of monocytes and production of cytokines (8). Hyperglycemia and dyslipidemia that last for an extended time both contribute to oxidative stress rise, which increases the production of oxidized low-density lipoprotein, stimulates immunological cells, and increases the levels of VCAM-1 and ICAM-1, which contribute to the creation of foam cells (9). Many researches demonstrated that VCAM-1 and ICAM-1 are involved in the development of microvascular issues (10,11). The purpose of this study was to determine the levels of VCAM-1 and ICAM-1 in T2DM with and without dyslipidemia, the findings of which may be helpful in the follow-up care of diabetic patients with dyslipidemia and in preventing the development of CVD.

## Patients and Methods:

One hundred and fifty participants were included in the study with an age range of (35-55) years. They were divided into three groups: Group 1 (G1) consisting of 50 healthy individuals (control group), Group 2 (G2) consisting of 50 T2DM patients with no

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dyslipidemia, and Group3 (G3) consisting of 50 T2DM patients with dyslipidemia. Venous blood samples (5 milliliters) were collected from each participant in the three groups from November 2022 to April 2023 at the National Center for Diabetes Treatment and Research, Baghdad, Iraq. The blood samples were used to measure HbA1C by the fluorescence immunoassay technology and the levels of VCAM-1 and ICAM-1 by the ELISA test (Mybiosource / USA). The concentrations of serum FBG, TG, TC, and HDL were determined by manual procedures. The Statistical Packages of the Social Sciences, version 21 (SPSS-21) was used for statistical analysis, with  $P < 0.05$  accepted as significant. Quantitative variables were correlated using Pearson's correlation. The t-test was used to test the difference between two independent means. The evaluations of the Receiver Operating Characteristic

(ROC) curves were investigated for the three study groups for VCAM-1 also ICAM-1.

**Results:**

The results of the FSG, HbA1c, TG, also HDL tests are shown in table (1). There was a significant difference between the means of FBG and HbA1c in G2 and G3 compared to G1. No such difference was found between G3 and G2. The table also shows that the mean TG level in G3 (237.9 ng/mL) was significantly higher than in G1 (93.5 ng/mL) and G2 (101.5 ng/mL). The means of G2 and G1 were not significantly different. The mean TC levels in G1 (156.1) and G2 (157.3 ng/mL) were significantly higher than in G3 (216.0 ng/mL). However, the difference between G2 and G1 was not significant. compared to G2 and G1, the mean HDL level in G3 was significantly lower. The mean levels of G2 and G1 were not significantly different.

**Table 1: Mean levels of FBG, HbA1c, TG, TC, and HDL in the three study groups**

Parameter	Mean ± SD			p-value		
	G1_n (50)	G2_n (50)	G3_n (50)	G1&G2	G1&G3	G2&G3
FBG (mg/dL)	89.0±8.82	184.5±8.41	211.5±8.29	S	S	NS
HbA1c%	4.9±0.43	8.5±1.95	8.8±1.79	S	S	NS
TG (mg/dL)	93.5±15.77	101.5±33.89	237.9±51.88	NS	S	S
TC (mg/dL)	156.1±26.3	157.3±33.14	216.0±35.54	NS	S	S
HDL (mg/dL)	51.5±7.41	46.2±10.90	31.2±4.45	NS	S	S

Table (2) shows the mean levels of VCAM-1 and ICAM-1 for the three groups. As for VCAM-1, G3 and G2 had significantly higher levels than G1. The

mean for G3 is higher than G2. The mean levels of ICAM-1 for G2 and G3 were higher than for G1, but they were not significantly different for G2 and G3.

**Table 2: The mean levels of VCAM-1 and ICAM-1 in the three study groups**

Parameter	Mean±SD			p-value		
	G1_n=(50)	G2_n=(50)	G3_n=(50)	G1&G2	G1&G3	G2&G3
VCAM-1 ng/mL	1014.3±136.5	2326.1±720.52	2888.2±722.15	S	S	S
ICAM-1 ng/mL	1.7±0.12	2.8±0.53	2.6±0.39	S	S	NS

**Correlation of VCAM-1 and ICAM-1**

Table (3) and figure (1) show a highly significant positive correlation between VCAM-1 and ICAM-1 in G1 ( $r = 0.531$ ) and G2 ( $r = 0.381$ ). A negative non-significant correlation was found in G3 ( $r = -0.131$ ).

**Table 3: Correlation coefficients between VCAM-1 and ICAM-1 in the three study groups**

Parameters	VCAM-1		
	G1	G2	G3
ICAM-1	$r = 0.531$ (HS)	$r = 0.381$ (S)	$r = -0.131$ (NS)

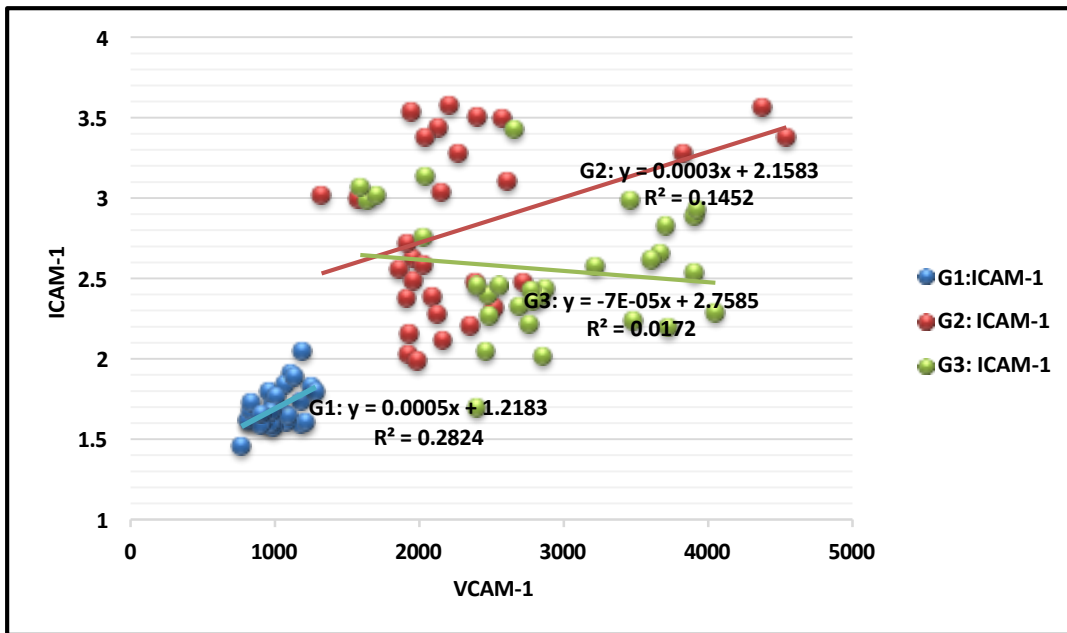


Figure (1): Correlations between VCAM-1 and ICAM-1 in the three study groups

**Receiver Operating Characteristic (ROC):** For VCAM-1: ROC curve analysis of VCAM-1 in the three study groups reveals an impressive area under the curve (AUC) of 0.87, which is significant at 95% with a p-value of 0.0081, that is less than the 0.01 threshold. The VCAM-1 optimal cut-off value is 1926. The sensitivity and specificity were 91% and 86%, respectively, as shown in table (4) and figure (2). The results demonstrate high accuracy levels in discriminating between the three groups, and the efficacy of the VCAM-1 test among three groups.

1- For ICAM-1: ROC curve analysis shows a value of 0.76 AUC that is significant at 95% with a 0.007 p-value, which is less than the threshold of 0.01. The ICAM-1 optimal cut-off value was 2.23. The sensitivity and specificity were 90% and 73%, respectively. This shows a high accuracy in recognition between the three groups and the test efficacy among the groups, table (4) and figure (3).

Table 4: sensitivity and specificity for VCAM-1

Variables	Statistical Values		Area under the curve	Accuracy		Cut off value
	Sensitivity	Specificity		L.B.	U.B.	
VCAM-1	0.91	0.86	0.87	0.79	0.95	1926

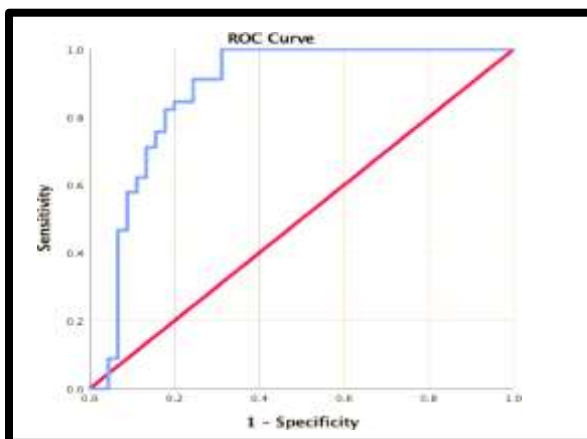


Figure (3): ROC for ICAM-1

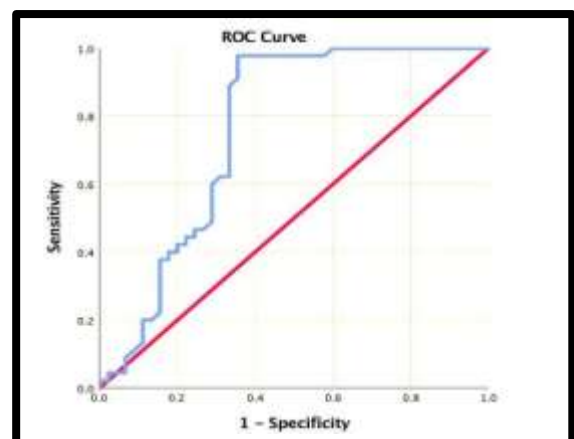


Figure (2): ROC for VCAM-1

### Discussion:

The findings of the current study, reveal that diabetic patients had greater levels of FBG and HbA1c than the control which is supported by a number of other investigations (12–14). This may indicate that those diabetics were not well-controlled.

Several studies have indicated that diabetics have greater rates of dyslipidemia, a condition that is related to hyperglycemia, increased HbA1c in blood, and hypercholesterolemia (15). This condition affects the ability of the body to process fats. Diabetics have abnormal lipid profiles and high HbA1c levels (16, 17). The abnormalities of lipids include low HDL and high TG and TC (18, 19). The findings of the current study agree with previous studies which showed that dyslipidemia is more common in T2DM cases (20–22). Dyslipidemia contributes to CVD development due to the persistent buildup of lipid plaques on arterial walls (23,24).

The findings on the effect of HDL on the upregulation of VCAM-1 messenger RNA inside human umbilical vascular endothelial cells were recently made public with participants representative of the general population (25).

Adhesion molecules presence in diabetics without micro- or macro-vascular complications indicates that the endothelium is functioning, but is bound to release endothelial products, that are linked to microangiopathy development (26,27).

The levels of ICAM-1, VCAM-1, and HbA1c were shown to have a significant correlation in a recent study that measured glycemic control. Since prolonged uncontrolled hyperglycemia makes glycemic control more difficult, the levels of these molecules are greater when there is poor glycemic control (28). According to the findings of other studies, the levels of VCAM-1 in the isolated endothelial cells of diabetes patients are much greater than those of ICAM-1. This result is consistent with the concept that diabetics who have the consequences of their illness, such as macrovascular and diabetic renal disease, should have greater levels of VCAM-1 (29,30).

A recent study found that persons who had greater ICAM-1 and VCAM-1 showed higher TGs and lower HDL levels. Despite the importance of these molecules in the progression of atherosclerosis in diabetic and cardiovascular patients, studies indicated that the higher the levels of VCAM-1 and ICAM-1 the higher the risk of T2DM in individuals (31,32).

### Conclusions:

VCAM-1 and ICAM-1 are potentially significant factors in the development of dyslipidemia in diabetes patients. They might serve as biomarkers to accurately predict the progression of cardiovascular disease.

### Authors' declaration:

We hereby confirm that all Figures and Tables in this manuscript are ours. Besides, the figures and images, which are not ours, have been given permission for re-publication and attached to the manuscript.

Ethical Clearance: The institutional Scientific Committee at the National Diabetes Center/ Mustansiriyah University approved this study according to the Declaration of Helsinki for human studies (Consent number: 1501 on 14/11/2022).

**Conflicts of Interest:** None

**Funding:** None

### Author Contributions:

Study conception & design: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei). Literature search: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei). Data acquisition: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei). Data analysis & interpretation: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei). Manuscript preparation: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei). Manuscript editing & review: (Abbas M. Alsaedy & Zeinab M. Al-Rubaei).

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### دراسة جزيئات الالتصاق في المرضى العراقيين المصابين بداء السكري من النوع الثاني وإضطراب شحميات الدم

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#### الخلاصة:

**الخلفية:** جزيئات الالتصاق الخلية هي كيانات بروتينية موجودة على سطح الخلايا. لقد ثبت أن التعبير عن جزيء التصاق الخلايا الوعائية (VCAM-1) وكذلك جزيء الالتصاق بين الخلايا (ICAM-1) مرتبط بإضطراب شحميات الدم وكذلك داء السكري من النوع الثاني. **الأهداف:** تحديد مستويات VCAM-1 و ICAM-1 لدى مرضى اضطراب شحميات الدم السكري ومعرفة ما إذا كانت هناك علاقة بين مستويات VCAM-1 و ICAM-1 مع تطور اضطراب شحميات الدم لدى المصابين بداء السكري من النوع الثاني.

**المرضى والمنهجية:** شملت الدراسة 150 شخصاً: خمسين من الأصحاء (المجموعة الأولى - G1)، خمسين مريضاً بداء السكري من النوع الثاني (المجموعة الثانية - G2)، وخمسين مريضاً بداء السكري من النوع الثاني مع اضطراب شحميات الدم (المجموعة الثالثة - G3). تم سحب الدم الكامل لغرض قياس نسبة HbA1c، وفصل المصل لغرض قياس سكر البلازما الصائم، الدهون الثلاثية، الكوليسترول الكلي، البروتين الدهني عالي الكثافة بالطرق اليدوية، بينما تم قياس VCAM-1 و ICAM-1 عن طريق اختبار ELISA. أجريت الدراسة في الفترة ما بين نوفمبر 2022 وأبريل 2023 في المركز الوطني لعلاج وأبحاث السكري، بغداد، العراق.

**النتائج:** أظهرت النتائج ارتفاعاً معنوياً في مستويات سكر البلازما الصائم و HbA1c في G2 و G3 مقارنة بـ G1، مع زيادة غير معنوية في G3 مقارنة بـ G2. أظهرت النتائج الحالية ارتفاعاً معنوياً في مستويات الدهون الثلاثية والكوليسترول الكلي في G3 مقارنة مع G1 و G2، في حين لوحظت زيادة غير معنوية في G2 مقارنة مع G1. أظهرت مستويات البروتين الدهني عالي الكثافة انخفاضاً معنوياً في G3 مقارنة مع G1 و G2، بينما لم تظهر فروق معنوية في G2 مقارنة مع G1. وجدت زيادة مستويات VCAM-1 و ICAM-1 بشكل ملحوظ في G2 مقارنة بـ G1، وزيادة VCAM-1 بشكل ملحوظ في G3 مقارنة بـ G2 في. وجدت فروق غير معنوية في G3 مقارنة مع G2 في مستويات ICAM-1.

**الاستنتاجات:** قد يكون هناك دور مهم لـ VCAM-1 و ICAM-1 في مسببات اضطراب شحميات الدم لدى مرضى السكري ويمكن اعتبارهما كمؤشر حيوي للتنبؤ بتطور أمراض القلب والأوعية الدموية لدى هؤلاء المرضى.

**الكلمات المفتاحية:** داء السكري، اضطراب شحميات الدم، VCAM-1، ICAM-1.