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# Association of soluble vascular cell adhesion molecule -1 (sVACAM-1) with cardiovascular disease and glycemic control among type 2 diabetic patients

Iman Jabbar Kadhim<sup>1</sup>, Suaad Muhammed Rasheed<sup>1</sup>, Falah Abdulhasan Deli<sup>2</sup>, Shaymaa Abdullateef Alfadhul<sup>1</sup> <sup>1</sup>COMMUNITY MEDICINE, FACULTY OF MEDICINE, UNIVERSITY OF KUFA, KUFA, IRAQ <sup>3</sup>INTERNAL MEDICINE, WARITH ALANBYAA COLLEGE OF MEDICINE, BAGHDAD, IRAQ

#### ABSTRACT

**Aim:** This study aimed to assess the Association of sVACAM-1 with type 2 diabetes mellitus and the impact of cardiovascular disease and glycemic control on its level. **Materials and Methods:** This is a study of sVACAM-1 level in 57 patients with type 2 Diabetes mellitus in Al-Najaf/Iraq in comparison with normal control, the level of sVACAM-1 was analyzed also according to parameters of age, sex, smoking, body mass index (BMI), presence of systemic hypertension and cardiovascular diseases (ischemic heart disease and heart failure), Poor diabetic control (Hemoglobin A1C  $\geq$ 7) and the mean of 2 days postprandial blood sugar **Results:** All parameters except smoking were associated with higher levels of sVACAM-1, however the differences weren't significant statistically, there was no linear correlation between the mean 2 days post prandial blood sugar and sVACAM-1

Conclusions: sVACAM-1 is important to be assessed in diabetic patients and recommended to establish cutoff values of normality

KEY WORDS: Type 2 Diabetes mellitus; sVACAM-1; glycemic control; HbA1c

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#### INTRODUCTION

Diabetes mellitus is an important medical problem globally with significant morbidity and mortality impact that differs in severity between different communities, the adverse outcome related primarily to the state of control and consequently the acute and most importantly the chronic complications, situation is becoming more concerning as the number of affected individuals approaches half a billion [1]. Immune and inflammatory processes had been well elucidated in type 1 Diabetes mellitus, whereby several autoantibodies are incriminated to be the primary cause of islet cell destruction and consequently hyperglycemia due to insulin deficiency, but more notably is the rapidly emerging discovery of several inflammatory mediators that contribute to multi-organ damage, primarily affecting the vascular system, including both microvascular and macrovascular structures and these vascular changes are the important causes for morbidities as blindness, atherosclerotic cardiovascular diseases and renal involvement and mortality, these inflammatory processes are not restricted to type 1 diabetes mellitus but are

also well documented in type 2, and the problem is more serious as type 2 is more prevalent and it has a preclinical or premorbid state than can be prolonged for more than a decade, during this period where the diabetes is out of control, vascular changes can progress hence the patient may have end organ damage at time of diagnosis [1,2].

Animal studies in the twentieth century revealed clearly the association of different inflammatory markers and diabetes, hyperglycemia as well as obesity were found to increase the markers like tumor necrosis factor -alpha, human studies as well documented this association and several other markers are incorporated including different interleukins, cytokines, plasminogen activator inhibitor 1 and C reactive protein [3]. Important markers promoting vascular damage are the adhesion molecules including vascular cell adhesion molecule-1 (VCAM-1) and the selectins (P and L types) these are increased in expression by TNF- $\alpha$ , consequently this will increase the interaction between cells of endothelium and leucocytes [4].

sVCAM-1 belongs to immunoglobin superfamily which includes also auto antibodies and receptors of T

lymphocytes, sVCAM-1 has an important role in pathogenesis and progression of atherosclerosis and found to be increasing in different autoimmune disorders like rheumatoid arthritis where it was presumed to be enrolled in increasing disease severity and cardiovascular complications [5].

sVCAM-1 expression was found to be increased in diabetic patient with different types of vasculopathy, microvascular occlusion by recruited and adhered leucocytes and platelet aggregate to capillary endothelium with the resultant increased capillary permeability ultimately leads to progression of diabetic retinopathy [6-8].

In other diabetic vasculopathy sVCAM-1 and selectins were also increased in expression and these includes diabetic nephropathy, diabetic neuropathy and diabetes mellitus in association with coronary heart disease and systemic hypertension [9-11].

## **MATERIALS AND METHODS**

STUDY DESIGN, SETTING, AND POPULATION This is a case control study done at Alsadr teaching hospital / AL Najaf/ during the period from January till July 2024, 57 patients with type 2 diabetes mellitus who are on medical treatment for at least 3 years, and 47 age, sex and body mass index (BMI) matched non diabetic healthy persons were taken as a control group, all the included study population were initially assessed regarding age, sex, duration of the disease, the presence of documented and treated systemic hypertension and the history of cardiovascular disease including ischemic heart disease (IHD) and heart failure (HF), all patients were assessed by a physician and their previous medical reports were analyzed thoroughly

## AIM

This study aimed to assess the Association of sVACAM-1 with type 2 diabetes mellitus and the impact of cardio-vascular disease and glycemic control on its level.

#### STUDY SIZE ASSESSMENT

The study size was assessed by the department of CME and scientific research of the Faculty of Medicine/ University of Kufa after analysis of the proposal of the study

Table 1. Serum sVACAM-1 mean level among type 2 diabetic patients and healthy controls

	Patients n = 57	Healthy control n = 47	P value
sVACAN	Л-1 (pg/ml)		
Mean± SD	6.75± 3.40	5.84± 1.22	0.086 †
Range	5.00 - 29.00	1.67-8.02	-

Table 2. The mean serum levels of sVACAM-1 regarding sociodemographic and clinical characteristics of diabetic patients

Characteristics		Ν	Mean	SD	Ρ
Age groups	< 50 years	7	6.32	1.18	0.729 a
	50-59 years	15	6.27	1.51	
	≥ 60 years	35	7.03	4.20	
Sex	Male	33	6.30	1.36	- <b>0.247</b> †
	Female	24	7.36	4.99	
Smoking	Positive	18	6.16	0.91	- 0.378†
	Negative	39	7.02	4.05	
Duration of disease	< 10 years	22	6.13	0.91	- 0.238†
	≥ 10 years	35	7.13	4.26	
BMI	None obese	29	6.17	1.37	- 0.197†
	Obese	28	7.34	4.62	









**Fig. 2.** Mean serum VACAM-1 level difference regarding cardiovascular diseases (ischemic heart disease and heart failure) among diabetic patients

**Fig. 3.** Mean serum VACAM-1 level difference regarding glycemic control among diabetic patients

## STUDY EXPOSURES

BMI was calculated using the application MD+CALC based on BMI=weight (kg)/square height (meter)

The following blood tests were done

 Hemoglobin A1C for both groups, uncontrolled diabetes was defined as HbA1C ≥ 7% [1]



Fig. 4. Linear correlation between 2 days mean postprandial blood sugar and sVACAM-1

- 2- Two samples of blood sugar of 2 hours post usual breakfast for the patients' group and one fasting and one 2 hours post breakfast samples for the control group
- 3- Serum sVACAM-1 for each group was assessed by a single test for each participant applying kits of BT LAB (Bioassay Technology Laboratory)

#### STATISTICAL ANALYSIS

Statistical analysis was done utilizing SPSS of IBM versionindependent Student's t-test and Pearson's linear correlation were applied at appropriate places and P values were considered significant at level <0.05

#### ETHICAL CONSIDERATION

Ethical approval for the study was obtained from the Ethical Committee of the Faculty of Medicine, University of Kufa. Verbal consent was obtained from all participants.

#### RESULTS

In this study the mean sVACAM-1 was higher in diabetic patients ( $6.75\pm 3.40$ ) compared to control group ( $5.84\pm 1.22$ ), however, these differences were not statistically significant, (table 1).

Age above 60 years, Female sex, increased duration of the disease and obesity were associated with higher

S VACAM-1 among diabetic patients, the differences were not significant statistically as shown in table 2, nonsmokers had less s VACAM as compared to smokers in this study, also the difference was not significant (table2).

According to Fig. 1, the presence of hypertension in diabetic patients was associated with a noticeable but non-significant increase in sVACAM-1. A similar trend was observed in diabetic patients with cardiovascular diseases (IHD or HF) (Fig. 2)).

Regarding diabetic control, patients with HbA1C  $\geq$  7% had higher sVACAM-1 levels, but the difference was not statistically significant (Fig. 3). No linear correlation was found between the 2-day mean RBS and sVACAM-1 (Fig.4)).

### DISCUSSION

Diabetes mellitus, a common and rapidly growing medical problem, especially in developing countries, is a multisystem disease [13]. Long-term complications and survival are largely determined by glycemic control—tighter control leads to better outcomes in terms of morbidity and mortality. Long-standing inadequate control and prolonged hyperglycemia affect several homeostatic mechanisms, impacting multiple tissues, organs, and systems, primarily due to glycation end products [14]).

Vascular endothelial dysfunction plays a crucial role in this process, as it is linked to accelerated atherosclerosis, ultimately leading to atherosclerotic cardiovascular diseases, including systemic hypertension and ischemic heart disease. Endothelial injury is associated with increased release of various adhesion molecules, including sVCAM-1, as well as L- and P-selectins. These molecules contribute to the aggregation and adhesion of inflammatory cells such as lymphocytes, macrophages, neutrophils, and platelets to the vascular endothelium, thereby exacerbating damage.

Several researchers have documented increased levels of these adhesion molecules in diabetic patients and, moreover, a possible further increase with prolonged disease duration, worsening diabetic control, and the presence of complications. However, due to the novelty of these markers and the lack of clearly established cutoff values, studies are limited, and results remain conflicting.

Ousamha A. Saterr et al. found increased sVACAM-1 levels in diabetic patients compared to healthy controls, with a significant further increase in those with cardiovascular diseases. Their study focused on patients with type 1 diabetes mellitus, and, surprisingly, serum VACAM-1 levels were extremely high, which was not observed in our study [15].

In this study, female gender, disease duration of more than 10 years, and obesity were associated with higher sVACAM-1 levels. However, these differences were not statistically significant, possibly due to the previously mentioned issue of the lack of an established cutoff value, which affects statistical analysis. Smoking, on the other hand, increases the level of sVACAM-1 and which possibly reflects the atherosclerotic potential of smoking on vessels. Surprisingly no such finding had been reported in this study! [16,17].

Most researchers agree on the effect of concomitant hypertension and cardiovascular diseases on the level

of sVACAM-1 in diabetics, the same effect was found in this study, however, the differences were not significant statistically [18]. Despite the nonsignificant association between high HbA1C, a marker of inadequate diabetes control, and the level of sVACAM-1, the difference is worth considering, and this is consistent with most other studies. The rise in HbA1C reflects the state of diabetes control over an extended period of 2-3 months. An important observation in the current study is the acute loss of control, as shown by the mean RBS of two postprandial readings. This has no relation to an increase in sVACAM-1 levels. Therefore, it can be concluded that changes in this marker are related to subacute and chronic variations in diabetes control. We found no related studies on this issue in the literature review.

## CONCLUSIONS

- 1. sVACAM-1 is important for assessment in diabetic patients with emphasis to assess the relation of control and cardiovascular issues on its levels.
- A thorough workup is needed to better define the cutoff values of sVACAM-1 in different patients' population.

WHAT IS ALREADY KNOWN ON THIS TOPIC sVACAM-1 is increased in diabetic patients. sVACAM-1 levels are related to state of diabetic control.

#### WHAT THIS STUDY ADDS

sVACAM-1 is not related to smoking in diabetic patients. The need for standardization of sVACAM-1 cutoff levels.

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## **CONFLICT OF INTEREST**

The Authors declare no conflict of interest

## **CORRESPONDING AUTHOR**

#### Iman Jabbar Kadhim

University of Kufa Imad Sukar, block 18 H 2, 3101, Najaf, Iraq e-mail: iman.alghizzi@uokufa.edu.iq

#### **ORCID AND CONTRIBUTIONSHIP**

Iman Jabbar Kadhim: 0000-0002-4733-8485 A B C D E F Suaad Muhammed Rasheed: 0000-0003-1654-9076 A B C D Falah Abdulhasan Deli: 0000-0002-7605-4529 A B E F Shaymaa Abdullateef Alfadhul: 0000-0002-8466-8344 B C F

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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