

## Correlation of Vascular Adhesion Molecule in Subjects without Vascular Complication

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### Abstract

### Original Research Article

An established independent risk factor for Cardio Vascular Disease (CVD) is diabetes. Cardiovascular (CV) morbidity is a main burden in patients with type 2 diabetes mellitus (type 2 DM), with endothelial dysfunction as an early indicator of diabetic vascular disease that is linked to the presence of a low-grade vascular inflammation. Since CAM is an index of inflammatory endothelial activation, a assessor of conventional cardiovascular risk factor evaluating it in an early stage would reduce the burden of morbidity and mortality among the DM subjects. **Materials and Methods:** This is a cross sectional study where in 36 patients with no vascular complication, matched with 33 controls were selected from OPD of Department of General Medicine. The cases where diabetic for at least 1 year. VCAM-1 levels were estimated by commercial kit available from Ray Biotech Pvt. Ltd by ELISA method. **Result:** Diabetic subjects showed a higher levels of VCAM-1 than the Normal subjects. When correlation between the two groups were analysed, VCAM-1 showed significant correlation with the duration of diabetes ( $p=.002$ ,  $r=.494$ ). When genderwise correlation was plotted, it was seen that in diabetic female subjects the difference was significant ( $p=.007$ ,  $r=.523$ ) with respect to VCAM-1 molecule. **Conclusion:** Though the clinical manifestation of vascular complication is not identifiable, the simulation for the expression of VCAM-1 molecule is evident. Hence VCAM-1 may be used as an early marker for vascular complications.

**Keywords:** Diabetes, Cell adhesion molecule, Vascular Cellular Adhesion Molecule.

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## INTRODUCTION

Diabetes is considered as an established risk factor for heart disorders. Also it is understood to be a important cause of death among the diabetic subjects [1]. It is observed that when diabetic subjects attain clinical CVD, chances of their prognosis are less than those without hyperglycemia [2, 3]. The most common attributable factor for their mortality is endothelial dysfunction. This endothelial dysfunction is nothing but a low-grade vascular inflammation which is more prevalent in lost term hyperglycemic subjects. Subsequently this endothelial dysfunction contributes to the pathogenesis of micro and macrovascular complications like diabetic nephropathy, diabetic neuropathy and diabetic retinopathy will eventually leads to formation of atherosclerotic lesion over decades. In the earlier stages changes in endothelin-1(ET-1) in the endothelium occurs through the stimulation of leukocyte adhesion molecules [4, 5] thus begins the beginning of the vascular inflammation.

Cellular adhesion molecules (CAMs), are members of selectin family involved in recruitment of leucocytes to the site of inflammation and are constantly expressed on several cell types in normal conditions on the resting endothelium. However these get upregulated throughout the exposure to pro-inflammatory stimuli as in during atherogenesis [6] hence acts as a biomarker in vascular disease [7, 8]. In diabetic subjects sustained exposure to hyperglycemia trigger damages to the endothelium because of continuous oxidative stress [9]. Studies have shown that long term exposure to hyperglycemia has found to increase the level of endothelial dysfunction by raising the level of vascular cellular adhesion molecule. Since VCAM can reflect the inflammatory endothelial activation on long term exposure, a assessor of conventional cardiovascular risk factor evaluating it in an early stage would reduce the burden of morbidity and mortality among the DM subjects [10]. Hence estimating the VCAM would target in finding the risk

assessment of CVD in diabetic subjects who have not developed micro and macro vascular complications.

## MATERIALS & METHODS

This study involved 36 patients with no vascular complications from OPD of General Medicine from Mc Gann Teaching district hospital, Shimoga. Controls were selected based on age sex match. Hence 33 controls were recruited. All participants were unrelated subjects who met the inclusion criteria of the study (Male or Female out-patients aged between 30-65 years, Persons with good control over glycemic levels, History of type 2 diabetes for at least 1 year without any preexisting micro and macro vascular disorder and are on diet control or oral hypoglycemic drugs.) all other cases were excluded. Presence of microalbuminuria was ruled out by estimating MAU in urine. Any value less than 30mg/g Cr was considered to be Normoalbuminuria and was considered as free from diabetic nephropathy. Self-history of diabetic neuropathy and diabetic retinopathy was taken. This study was approved by the Institutional Ethical clearance board of our institute.

VCAM-1 levels were estimated by commercial kit available from Ray Biotech Pvt. Ltd by ELISA method. The RayBiotech Human VCAM-1 ELISA kit is an in vitro enzyme-linked immunosorbent assay for the quantitative measurement of human VCAM-1 in serum, plasma, and cell culture supernatants. This assay employs an antibody specific for human VCAM-1 coated on a 96-well plate.

## RESULTS

The demographic data of the study population when plotted (Table 1) showed that the diabetic subjects were little elder than the controls. The most of the subjects in the control group were known to be diabetic atleast more than a year. It was observed that in both the gender, the BMI was almost the same along with the other parameters like SBP, DBP.

The mean value of total cholesterol was comparatively high in the diabetic subjects than in the normal study group. Surprisingly female diabetic subjects had a higher level of good cholesterol than the normal female subjects.

It is well depicted that the levels of VCAM among the diabetic subjects was higher than in the normal subjects. Also female subjects had higher levels of VCAM than the males as shown in the fig 1.

Table 2 shows the correlation of all the variables of the study population with VCAM. A positive correlation was seen among all the parameters except HDL, in the general study population which was not statistically significant. Among diabetic subjects with respect to the HC, Weight, DBP, Total Cholesterol and HDL-cholesterol a non- significant correlation was seen. Only duration of the diabetes showed statistically significance ( $P=.002$ ,  $r=.494$ ).

Further when the study population was classified based on gender, among the females duration of the diabetes showed statistically significance ( $P=.007$ ,  $r=.523$ ) as shown in table 3. But this correlation was lost among the males as shown in table 4.

**Table-1: Demographic data of the study population**

	Male Diabetic	Male Normal	Female Diabetic	Female Normal
Age (years)	44.90 ± 6.00	39.5±6.76	45.96±6.88	40.11±6.50
Diabetes Since (months)	23.81±15.24	NIL	23.36±15.95	NIL
HC (Cms)	94.27±6.46	101.12±11.15	98.72±7.59	95.17±11.18
WC (Cms)	92.09±9.25	96.68±30.71	95.56±5.82	97.88±9.82
Ht (Cms)	158.36±13.82	159.5±10.05	144.48±6.35	150.76±7.44
Wt (Kgs)	67.45±10.60	73.12±15.05	60.63±7.26	62.88±13.64
BMI	27.13±4.49	28.68±5.21	28.98±2.32	27.58±5.06
SBP(mm of Hg)	111.81±18.34	123.5±9.72	124.88±22.24	114.17±8.67
DBP(mm of Hg)	80.90±12.21	78.25±7.79	77.96±12.48	76.58±5.03
Chol (mg/ dl)	206.27±31.87	165.06±41.07	215.52±36.68	170.11±41.94
HDL (mg/dl)	54±14.56	43±11.00	59.68±11.56	53.82±10.04

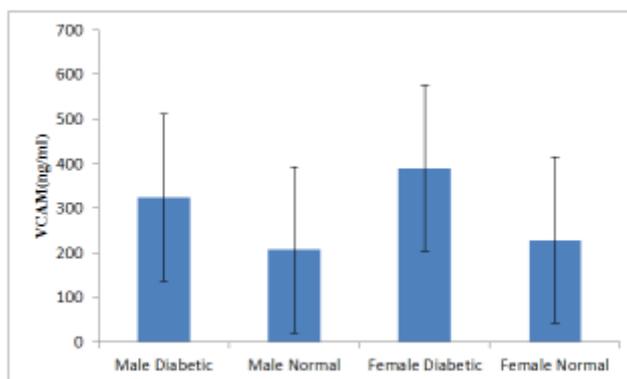


Fig-1: Levels of VCAM of the study population

Table-2: Correlation of Total study population

variable	Normal(VCAM) (n=33)		Diabetic(VCAM) (n=36)	
	*P	r	P	r
HC (Cms)	.997	.000	.164	-.237
WC (Cms)	.379	.158	.759	.053
Ht (Cms)	.410	-.148	.179	-.229
Wt (Kgs)	.555	.107	.312	-.173
BMI	.146	.259	.689	.069
SBP	.951	.011	.736	-.058
DBP	.764	-.054	.818	-.040
Cholesterol(mg/dl)	.733	.062	.968	-.007
HDL (mg/dl)	.227	-.216	.619	-.086
Duration of diabetes			.002	.494**

\*\* . Correlation is significant at the 0.01

Table-3: Correlation of female Total study population

variable	Normal(VCAM) (n=17)		Diabetic(VCAM) (n=25)	
	P	r	P	r
HC (Cms)	.726	-.092	.180	-.277
WC (Cms)	.966	-.011	.699	.081
Ht (Cms)	.205	-.324	.937	-.017
Wt (Kgs)	.965	.011	.708	-.079
BMI	.448	.197	.684	-.086
SBP	.998	.000	.955	.012
DBP	.072	-.447	.663	.092
Cholesterol(mg/dl)	.936	.021	.990	-.003
HDL (mg/dl)	.185	-.338	.389	-.180
Duration of diabetes			.007	.523**

\*\* . Correlation is significant at the 0.01

Table-4: Correlation of male Total study population

Variable	Normal(VCAM) (n=16)		Diabetic(VCAM) (n=11)	
	P	r	P	r
HC (Cms)	.514	.176	.362	-.305
WC (Cms)	.278	.289	.811	-.082
Ht (Cms)	.831	.058	.068	-.568
Wt (Kgs)	.242	.310	.343	-.316
BMI	.151	.376	.417	.273
SBP	.682	.111	.087	-.539
DBP	.225	.321	.174	-.442
Cholesterol(mg/dl)	.677	.113	.781	-.095
HDL (mg/dl)	.420	-.217	.876	.053
Duration of diabetes			.184	.432

\*\* . Correlation is significant at the 0.01

## DISCUSSION

A substantiated fact about diabetes mellitus is that it is associated with a greater risk of myocardial infarction, stroke, and peripheral artery disease. Hyperglycemia is an important risk factor for cardiovascular disease due to production of free radicals. These free radicals increase the expression of adhesion molecules, hence contributing to the development of vascular complication [9, 11]. In our study population the diabetic group had a higher value of VCAM than the normal study population. This is agreeing with the studies conducted by Hadi *et al.*

It is studied that there exists non-enzymatic coupling of glucose molecules with the lysine of the protein. This glycated protein is believed to have a strong adhering capacity to immunoglobulin or to the mechanism which activate the process of inflammation. Hence this causes the damage to the vascular endothelium [12, 13]. Also other known mechanism of causing vascular remodeling is over synthesis of reactive oxygen species, which are responsible for lipid abnormalities along with the release of pro-inflammatory cytokines and stimulation of rennin-angiotensin system [14].

When gender wise levels of VCAM were tabulated, it was observed that female had a higher level of VCAM than the males as shown in Figure 1. But this was contradicted by Ab *et al* where they reported a higher levels in females [15] this may be partly be explained on the basis that menopausal state and the treatment taken during post-menopausal like hormone replacement therapy influence the level of VCAM. In our study most of the female had not reached the menopausal state and hence the discrepancy. Also study by McCrohon *et al.* has shown that androgen exposure increases human monocyte adhesion to vascular endothelium and endothelial cell expression of vascular cell adhesion molecule is apparent, this may explain some protection among the women in premenopausal state in developing CVD [16].

Several studies have supported the idea of influence of lipid levels and statin therapy on expression of CAM. Studies have also shown that higher levels of cholesterol, LDL are known to increase the VCAM levels [17] [18]. But observational studies did not associate with the levels of cholesterol or LDL in three large studies which is similar to our observation. Also we found negative associations with HDL (table 2) which also agree with two studies [19, 20].

Our study showed a significant correlation between VCAM and duration of diabetes (table 2). Our study diabetic subjects had hyperglycemic state since 23 months and we assume that this duration was

sufficient to reflect the expression of VCAM levels. Further when gender wise correlation was tabulated, we still found significant correlation among the diabetic female subjects and no correlation was found in the diabetic male subjects (table 3&4). These changes may be due to hormonal effects [16].

A well-known fact is that expression of adhesion molecules correlate with BMI, in fact excess of adipose tissue exert a low grade of inflammation hence the effect [21]. But in our study there was no significant correlation between BMI or WC or HC and VCAM levels (table 3&4).

## CONCLUSION

Our group showed significant correlation only between duration of diabetes and VCAM. Which may explain that though the clinical manifestation of vascular complication are not nor apparent, the stimulation for the expression mere by exposure of hyperglycemic state is evident. This reveals the fact that interaction between VCAM synthesis and its role with respect to its concentration in the blood may elucidate the discrepancies among the mechanism and the clinical findings.

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## DECLARATIONS

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