



**CIRCULATING CELL ADHESION MOLECULES ARE
ELEVATED IN HIV + WOMEN**

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ABSTRACT

Background: Elevation of soluble cell adhesion molecules (CAMs) has been associated with atherosclerotic risk. We investigated relationships of intercellular cell adhesion molecule-1 (sICAM), vascular cell adhesion molecule-1 (sVCAM) and E-selectin with measures of body fat distribution, lipids and carbohydrate metabolism in HIV+ women

Methods: This cross-sectional study used samples which had been collected over a period of two years and stored frozen at -70°C . Abnormally distributed values were log transformed. ANOVA was used for comparisons among ethnic groups and treatment regimens. Pearson correlations were used for all other comparisons.

Results: The study population consisted of 74 women (66% Caucasian, 18% African American, 10% Hispanic and 6% other) 41 ± 7.9 years of age. Concentrations of sICAM, sVCAM and sE-selectin were elevated compared to published values but did not differ by race or treatment regimen (HAART+PI, HAART+NNRTI, NRTI only, no treatment) and were not related to time on treatment or time in storage. None of the CAMs correlated to WHR, BMI, insulin or glucose concentrations. All three CAMs were inversely related to LDL concentrations ($p < .05$). In addition, sICAM and sVCAM were inversely related with HDL₃ ($p < .001$ for both) and E-selectin was directly related to HDL₂ concentrations ($p < .01$).

Conclusions: Concentrations of cell adhesion molecules are elevated in HIV+ women and are related to lipoprotein concentrations. Further studies will be required to determine the mechanisms involved but the data suggest that these markers may reflect additional risk of vascular disease in HIV+ patients.

INTRODUCTION

Cell adhesion molecules (CAMs) are thought to play an important role in the initiation of atherogenesis. Several classes of CAMs mediate leukocyte adhesion and transmigration across the vascular endothelium. Intercellular cell adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) are members of the immunoglobulin superfamily and mediate cell adhesion. E-selectin is involved in leukocyte rolling and attachment on the endothelial leading to extravasation. Soluble forms of these molecules have been identified in the circulation and may be monitored as markers of inflammation and endothelial dysfunction (Springer 1990). Elevated levels of both classes of circulating CAMs are associated with increased risk of myocardial infarction, stroke, coronary artery disease and carotid atherosclerosis (Hwang et al 1997, Rohde et al 1998, Rohde et al 1999 and Ridker et al 2001). CAMs are also elevated in type 2 diabetes mellitus (Lampeter et al 1992, Devaraj and Jialal 2000). We sought to determine if levels of sICAM-s, sVCAM-1 and sE-selectin are elevated in HIV+ women and if levels correlate with metabolic parameters.

METHODS

Study Design: Cross-sectional

Samples: Serum which had been collected over a period of 2 years and stored frozen at -70°C.

Laboratory Analyses: sICAM and sVCAM, sE-selectin, sP-selectin and TNF α were determined in serum using ELISA kits purchased from R&D Systems, Inc (Minneapolis MN).

Data Analysis: Abnormally distributed values were log transformed. ANOVA was used for comparisons among ethnic groups and treatment regimens. Pearson correlations were used for all other comparisons.

RESULTS

Table 1: Characteristics of Study Subjects

N	74
Age (yr)	41 ± 8*
CD4 cells/ml	459 ± 232
PVL < 500 copies/ml (%)	66
BMI (kg/m ²)	27.0 ± 4.9
WHR	.88 ± .09
Glucose (mg/dl)	93 ± 30
Insulin μU/ml	23.3 ± 33.4
Total cholesterol (mg/dl)	204 ± 58
Triglycerides (mg/dl)	170 ± 92
LDL (mg/dl)	128 ± 48
HDL (mg/dl)	44 ± 16
HDL-2 (mg/dl)	16 ± 12
HDL-3 (mg/dl)	29 ± 7

*Mean ± SD

Table 2: CAM Concentrations by Ethnic Group

	sVCAM	sICAM	sE-Selectin
Caucasian	749 ± 330*	464 ± 199	64 ± 26
African American	671 ± 144	424 ± 239	72 ± 41
Hispanic	653 ± 320	539 ± 300	81 ± 53
Other	647 ± 238	483 ± 136	79 ± 31
All	701 ± 300	467 ± 210	68 ± 32
Control Women**	448 ± 123	274 ± 100	38 ± 18

* Mean ± SD; ng/ml

**Hwang et al. 1997

CAM concentrations do not differ among ethnic groups

Table 3: CAM Concentration by Treatment Group

	sVCAM	sICAM	sE-Selectin
PI	646 ± 236*	454 ± 195	68 ± 37
NNRTI	721 ± 361	457 ± 210	73 ± 37
NRTI only	770 ± 394	497 ± 275	63 ± 31
None	831 ± 225	500 ± 171	66 ± 24
All	701 ± 300	467 ± 210	68 ± 32

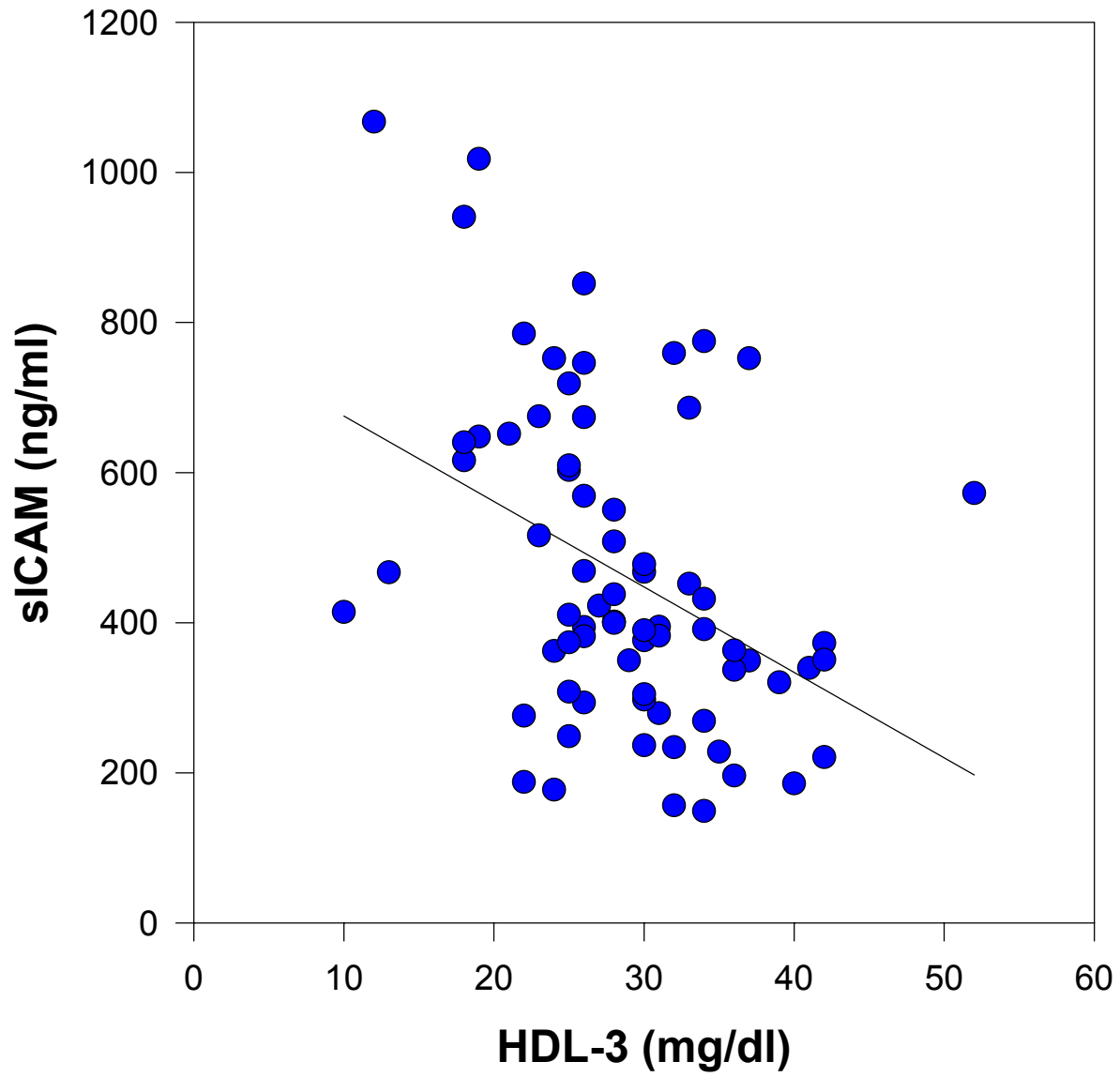
*Mean ± SD; ng/ml

CAM concentrations do not differ among ethnic groups

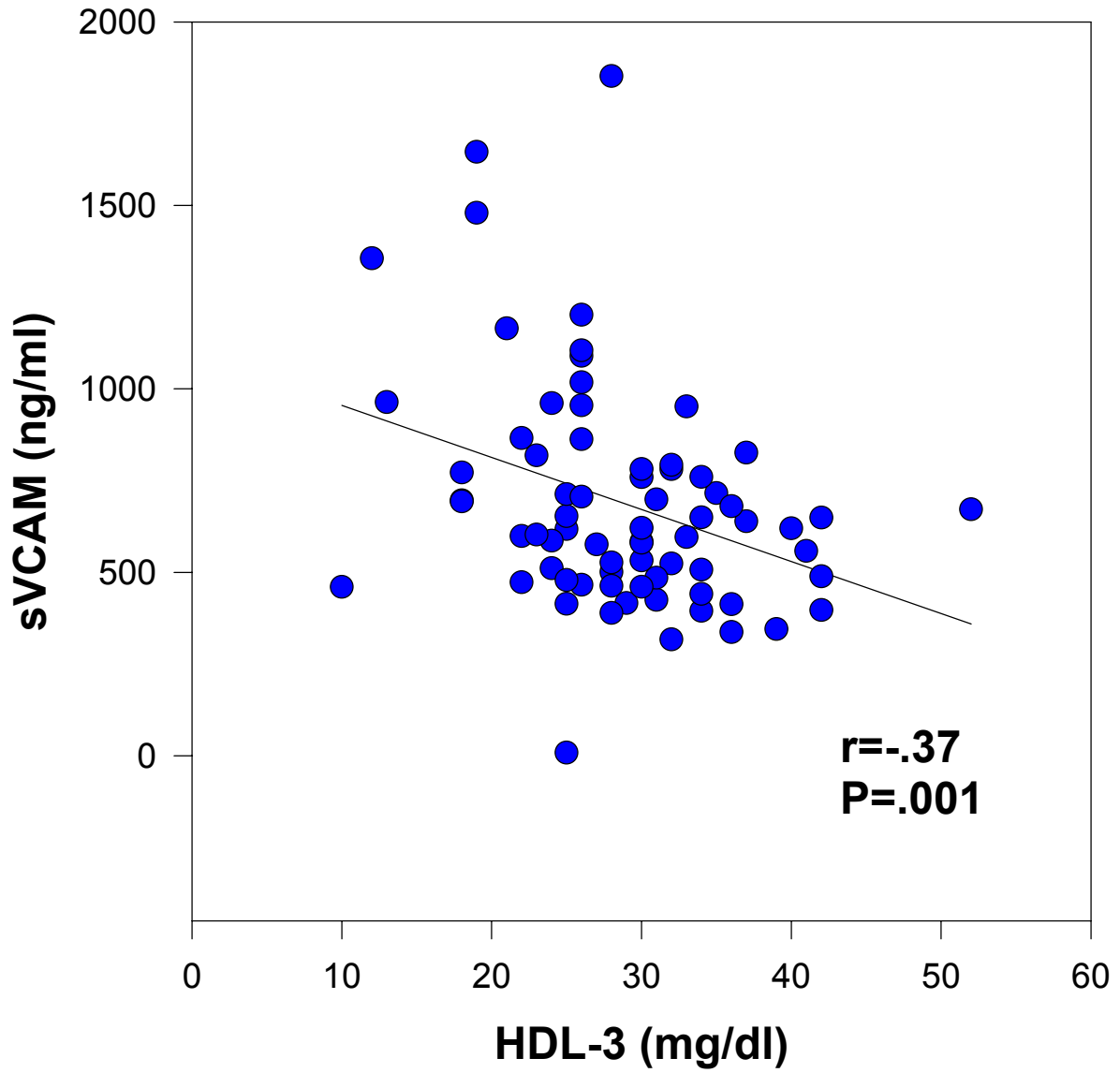
Table 4: Correlates of CAM Concentrations

	sICAM		sVCAM		E-Selectin	
	r	P	r	P	r	P
sICAM			0.657	<.001	0.479	<0.001
sVCAM	0.657	<0.001			0.447	<0.001
E-Selectin	0.479	<0.001	0.447	<0.001		
CD4	-0.404	0.012	-0.301	0.075	-0.013	0.94
HIV RNA	-0.005	0.98	0.166	0.33	-0.125	0.45
TNF α	-0.058	0.77	0.053	0.79	-0.063	0.75
BMI	-0.226	0.052	-0.126	0.32	-0.098	0.41
WHR	0.08	0.52	-0.082	0.52	0.11	0.37
Glucose	0.247	0.034	0.045	0.71	0.008	0.94
Insulin	0.18	0.13	0.027	0.82	0.203	0.09

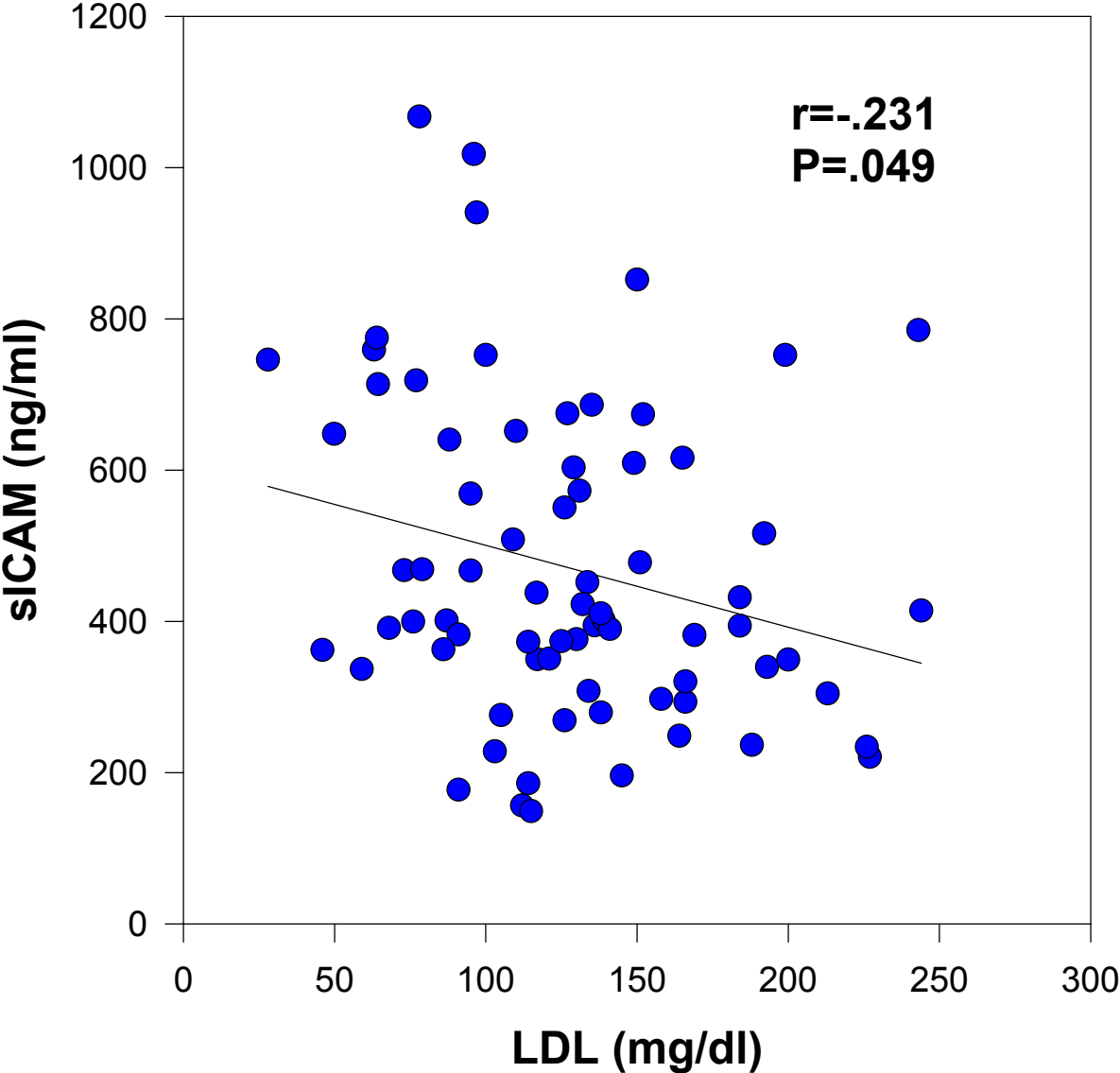
sICAM vs HDL-3



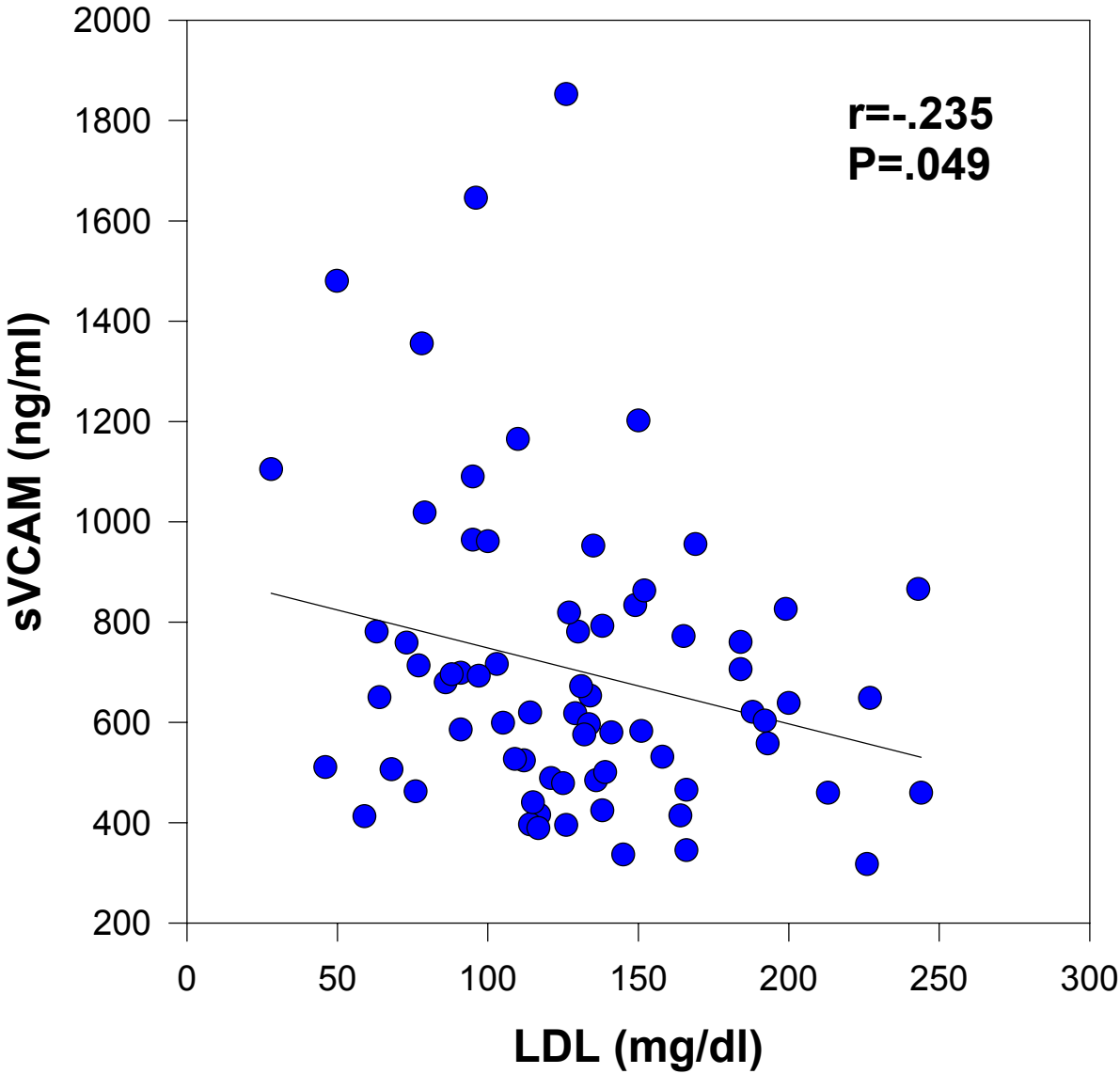
sVCAM vs HDL-3



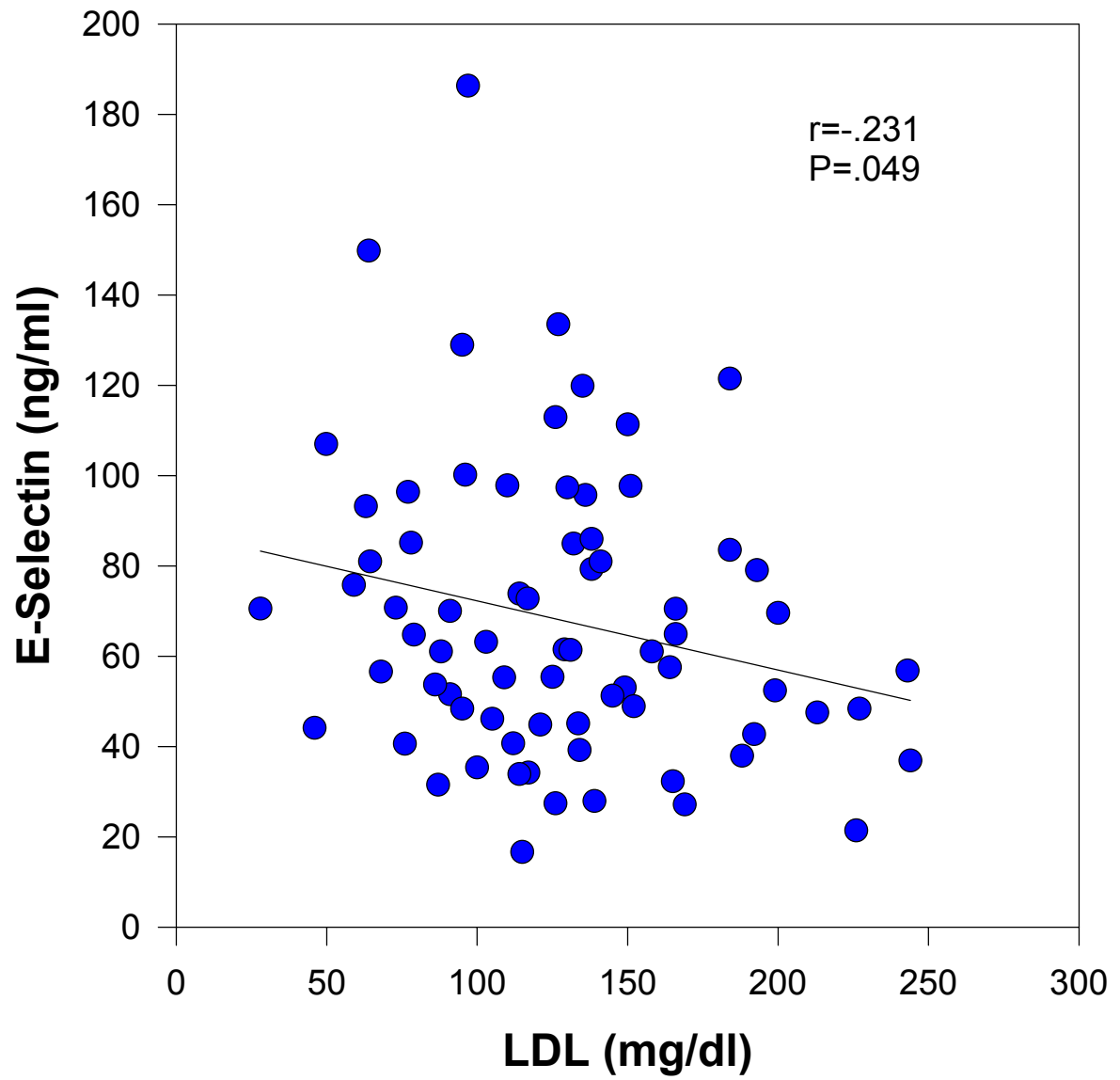
sICAM vs LDL



sVCAM vs LDL



E-SELECTIN VS LDL



SUMMARY

1. Concentrations of sICAM-1, sVCAM-1 and sE-selectin are elevated in HIV+ women compared to values reported for normal women (Rohde et al 1998)
2. Concentrations of sICAM, sVCAM and E-selectin do not differ by race or treatment regimen.
3. sICAM concentrations correlated with CD4 count. There were no correlations with HIV RNA or TNF α levels.
4. sICAM, sVCAM and sE-selectin are inversely related to LDL cholesterol and sICAM and sVCAM are inversely related to HDL-3 cholesterol

CONCLUSIONS

Elevated soluble cell adhesion molecule concentrations are elevated in HIV infected women and may increase the risk of vascular disease. Concentrations do not appear to be related to plasma viral load or cytokine TNF α concentration but are associated with lipoprotein levels. Further studies will be required to determine mechanisms involved in adhesion molecule elevations and their association with vascular disease risk in HIV+ populations.

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