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ASYMMETRIC DIMETHYLARGININE LEVEL and ATHEROSCLEROSIS MARKERS IN CUSHING'S SYNDROME

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OBJECTIVE

Cushing's syndrome (CD) is frequently accompanied by conditions that are associated with increased risk of cardiovascular disease (CVD) including diabetes mellitus (DM), dyslipidemia, hypertension (HT) and central obesity. It has been known that high cortisol levels lead to accelerated atherosclerosis, but the mechanism, is unknown. Asymmetric dimethylarginine (ADMA), lipoprotein-associated phospholipase a2 (LP-Pla2), homocysteine and highly sensitive C-reactive protein (hsCRP) levels were found to be significantly related with atherosclerosis. In addition, carotid intima-media thickness (CIMT) measurements, which reflect early atherosclerosis, and 'ankle-brachial index' (ABI) measurements, which demonstrate peripheral arterial disease, were also found in relation with atherosclerosis. The objectives of our study were to evaluate the well-known risk indicators of atherosclerosis such as ADMA, homocysteine, LP-Pla2, hsCRP, lipid levels, CIMT, and ABI measurements in patients with CS and to compare with co-morbid diseases matched control subjects. Our study included 27 patients with active CS and age, sex, body mass index (BMI) and co-morbid diseases (DM, HT and dyslipidemia) matched 27 control subjects.

Table 1: Baseline characteristics of CS and Control groups

	CS Group (n:27)	Control Group(n:27)	P
Age(years)	42.07 11.58	42 11.25	0.98
Gender(F/M)	24/3	24/3	1
BMI (kg/m²)	32.29 5.17	31.77 5.09	0.71
Waist circumference (cm)	112.56 10.66	107.67 14.13	0.51
Subcutenous fat thickness (cm)	1.32 0.33	1.43 0.46	0.30
FBG (mg/dl)	108.07(67-212)	105.00(70-191)	0.416
T. Cholesterol (mg/dl)	229.69±53.96	185.39±28.98	**0.001**
LDL-C (mg/dl)	136.80±43.23	113.86±20.08	**0.024**
HDL-C (mg/dl)	51.5 (32-59)	43 (30-57)	**0.004**
Triglyceride (mg/dl)	184.23±80.43	139.73±72.21	**0.04**
Apo A (mg/dl)	140.45±23.68	125.46±15.77	**0.01**
Apo B (mg/dl)	109.95±33.33	87.48±17.51	**0.006**
Lp-a (mg/dl)	10.90 (8.90-86.30)	9.69 (8.9-74.7)	0.343
hsCRP (mg/dl)	0.35(0.017-1.11)	0.37(0.031-1.11)	0.337
Homocysteine (µmol/lt)	16.63(9-50)	15.11 (9-35)	0.537
Lp.Pla2 (ng/ml)	21.71(3.11-89.5)	16.87(0,3-96)	0.085
ADMA (µmol/lt)	0.94 (0.63-1.47)	1.12 (0,36-1.64)	**0.013**
CIMT(n:25/27) (mm)	0.62 0.11	0.61 0.03	0.56
ABI	1.04 0.192	1.04 0.128	0.913

* Statistical analysis of T. Cholesterol, LDL-C, HDL-C, Triglyceride, Apo-A, Apo-B, Lp-a were performed after exclusion of the 5 cases who were on statin theraphy (n=25/24).

RESULTS

ADMA levels were statistically significant lower in the CS group compared to the control group (P=0,013). In the CS group, total cholesterol, LDL-C, triglyceride, HDL-C, Apo A and Apo B levels were higher rather than control group (p<0.05). There is no statistical difference between fasting blood glucose, hsCRP, LP-PLa2, homocysteine levels and CIMT, ABI in both groups (p>0.05). The correlation analysis in the whole study group was shown in Table 2. There was a positive correlation between ADMA level and fasting blood glucose (r=0.307, p=0.024). In the whole study group (n=54), factors associated with ADMA were evaluated with multiple stepwise linear regression analysis. 'The presence of CS' was found to be the main factor affecting ADMA levels (beta coefficient= -0.174, p= 0.012, r square= 0.116).

Table 2: Correlation between homocysteine, hsCRP, ADMA, Lp-PLa2, CIMT, ABI and other parameters in the whole group (n:54)

	hsCRP		Homosistein		ADMA		Lp.Pla2		CIMT		ABI	
	R	P	R	P	R	P	R	P	R	P	R	P
BMI	0.291	0.033	0.086	0.538	-0.022	0.877	0.084	0.545	0.135	0.340	-0.166	0.235
Waist circumference	0.274	0.045	0.098	0.480	-0.041	0.770	-0.048	0.731	0.078	0.583	-0.136	0.330
Subcutenous fat thickness	0.196	0.156	0.104	0.452	0.125	0.369	-0.109	0.432	-0.066	0.642	-0.040	0.774
FBG	-0.006	0.966	-0.148	0.285	0.307	0.024	-0.016	0.908	0.085	0.551	0.009	0.950
T.Cholesterol	-0.014	0.919	0.210	0.127	0.225	0.102	0.019	0.892	0.264	0.059	-0.130	0.352
LDL-C	0.126	0.365	0.135	0.329	0.158	0.255	0.072	0.605	0.181	0.199	-0.073	0.604
HDL-C	-0.046	0.740	0.185	0.179	-0.094	0.500	0.157	0.257	0.039	0.782	-0.079	0.575
Triglyceride	-0.128	0.357	0.110	0.427	0.210	0.127	-0.209	0.129	0.222	0.113	-0.113	0.421
Apo A	-0.140	0.312	0.129	0.354	-0.014	0.919	0.187	0.176	-0.021	0.883	-0.015	0.917
Apo B	0.080	0.563	0.168	0.226	0.189	0.171	0.046	0.742	0.171	0.224	-0.125	0.374
Lp-a	0.222	0.107	0.208	0.131	-0.268	0.050	0.078	0.574	0.076	0.593	-0.082	0.558

CONCLUSION

As a conclusion, we found that hsCRP, Lp-PLA2, homocysteine levels, CIMT and ABI measurements were similar between CS and comorbid diseases matched control groups. Our results suggest that atherosclerosis in CS may occur primarily due to comorbid diseases with CS. We found that ADMA levels were lower in CS, which should be further investigated.

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