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"Levels of AGEs (advanced glycation end products), sRAGE (AGE's receptor) and their relationship with cardiovascular risk factors in newly diagnosed type 2 diabetic patients“

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INTRODUCTION

Diabetes is associated with a greatly increased risk of cardiovascular disease and the advanced glycation end products (AGEs) and their receptors play an important role in these complications [1, 2, 3]. Detection of subclinical or preclinical atherosclerosis can be detected through non-invasive tests like carotid Intima Media Thickness (CIMT), Ankle brachial index (ABI) and flow-mediated dilation (FMD) [4, 5].

Studies in diabetic patients suggest as non-invasive tool to predicting atherosclerosis risk, the measuring of accumulation of AGEs in skin using fluorescence techniques (skin autofluorescence (SAF)). It has been observed that there are high levels of fluorescence in skin in patients with type 2 diabetes compared to healthy subjects and it is also directly related with the presence or development of microvascular complications [6].

OBJECTIVE

To study the association between AGEs and sRAGE levels with cardiovascular risk factors in obese and non-obese newly diagnosed type 2 diabetic patients.

MATERIAL AND METHODS

We conducted a cross-sectional study in subjects with type 2 diabetes mellitus of recent diagnosis, by means of a glucose tolerance test according to the ADA criteria (ages 35-65). We studied two groups, one with obesity (n=40) and other with normal weight (n=40). We measured somatometric variables, SBP, DBP, glucose, HbA1c, lipid profile, insulin, HOMA-IR, serum AGEs, ICAM-1, VCAM-1, 8-oxo-dG, MDA and, sRAGE. We also measured carotid intima-media thickness (cIMT) and flow-mediated dilation (FMD) by ultrasound.

RESULTADOS

We studied 80 patients and we divided them in two groups, normal weight (40 patients)and obese (40 patients) with average age: 48±7.3 years old.

Table 1
General, metabolic and cardiovascular risk characteristics in the study groups

CHARACTERISTIC	NORMAL WEIGHT n=40	OBESE n=40	T*/U[1]/X[2]	p
Demographic and anthropometric characteristics				
Age (years)*	50±15	49.2±9.9	0.442	0.7*
Gender[2]				
Women n (%)	27 (67)	28 (70)	0.483	0.3[2]
Men n (%)	13 (33)	12 (30)		
Weight (kg)	64±16	88.5±31.5	-7.108	<0.000[1]
Size(m)	1.63±0.17	1.545±0.205	1.601	0.6*
BMI (Kg/m^2)	22.97± 2.73	41.7±11.7	-7.706	<0.000[1]
Systolic blood pressure (mmHg)	120±7	124±6	-1.520	0.1[1]
Diastolic blood pressure (mmHg)	76±8	78±7	-0.937	0.7*
BIOCHEMICAL VARIABLES				
Glucose (mg/dl)	140.9±40.4	144.6±47.4	-0.372	0.6*
HbA1c (%)	6.6±1.6	7.6±1.3	-1.719	0.4*
Triglycerides(mg/dl)	198.15±98.2	234.3±150.8	-1.591	0.2*
Cholesterol(mg/dl)	213.1±88.1	220.6±72.6	-2.902	<0.004[1]
HDL -C(mg/dl)	66.6±19.6	60.2±10.3	-0.785	0.5*
LDL -C(mg/dl)	106.2±38.6	114.95±26.5	-2.522	<0.01[1]
VLDL-C (mg/dl)	39.6±19.6	46.85±30.15	-1.634	0.14*
ICAM-1 (ng/mL)	224.6±36.1	278.5±65.9	-3.714	<0.000[1]
VCAM-1 (ng/mL)	623.9±116.6	764.6±174.5	-3.714	<0.0001[1]
8-oxo-dG (nM)	52.7±8.3	66.91±17.4	-3.993	<0.0001[1]
MDA (nmol/mL)	818.5 ± 519.2	1635.9±1017.7	-3.719	<0.0001[1]
Insulin (uU/ml)	6.8±2.7	9.8±2.9	-3.714	<0.0001[1]
HOMA- IR	2.4±1.4	3.4±1.2	-3.214	<0.001[1]
TOTAL AGES (UA)	938.7±455.8	1302.3±611.9	-4.369	<0.0001[1]
CML (ng/mL)	14.7±6.1	22.7±13.9	-5.350	<0.0001[1]
CML-NY (u/mL)	12.0±2.5	16.2±4.6	-4.470	<0.0001[1]
sRAGE (pg/mL)	857.5±358.2	1197.9±404.1	-3.714	<0.0001[1]
CARDIOVASCULAR RISK CHARACTERISTICS				
Carotid intima media thickness (CIMT) (mm)	0.9±0.25	1.1±0.21	-3.205	<0.001[1]
Flow-mediated dilation in the brachial artery (FMD) (%)[2]	24.6±14.8	15.4±10.9	558.0	0.02[2]
Rigidity index	3.2±2.2	4.2±2.4	-2.608	<0.009[1]
Ankle branchial index (AAI)	0.99±0.08	0.96±0.07	1.113	0.6*
Skin autofluorescence(UA)	2.16±0.47	2.19±0.28	0.096	0.2*
Framingham Risk Score (%)[2]	7.4±3.9	8.02±3.0	23.4	0.1[2]
DIETARY VARIABLES				
Dietary AGES (KU)	9623.1±923.6	10,776.2±1121.9	-5.02	<0.015*
Food Energy(Kcal)	2548.9±267.4	3484.2±347.7	12.5	<0.0001*
Proteins	110.1±21.91	137.3±79.2	-0.010	0.1[1]
Carbohydrates	339.7±48.1	257.3±187.9	-2.539	<0.011[1]
Lipids	83.0±31.2	282.9±404.4	-6.865	<0.0001[1]

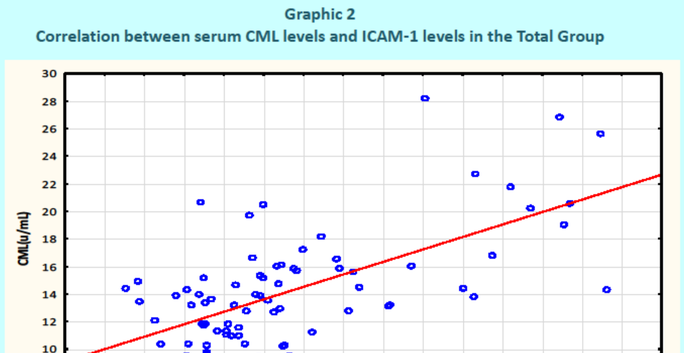
Table 2
Factors associated with Skin autofluorescence

TOTAL GROUP			
SIGNIFICANT VARIABLES	β	T	p
Carotid intima media thickness (CIMT)	-0.401914	-3.59827	<0.0001
HOMA-IR	0.337958	3.03003	<0.001
sRAGE	0.231512	2.76447	<0.001
Ankle branchial index (AAI)	-0.163788	-1.98921	<0.05
BMI			P
NO SIGNIFICANT VARIABLES	β	T	
Carotid intima media thickness (CIMT)	0.179603	1.77489	0.08
Framingham Risk Score	0.145122	1.72310	0.09
8-oxo-dG	-0.432643	-1.65916	0.1
HDL-C	-0.155347	-1.65689	0.1
Cholesterol	0.127630	1.31372	0.2
ICAM-1	0.364165	1.18105	0.2
OBESE GROUP			
SIGNIFICANT VARIABLES	β	T	P
Framingham Risk Score	0.72309	3.02838	<0.005
8-oxo-dG	-2.33385	-2.51903	<0.01
Carotid intima media thickness (cIMT)	-0.35325	-2.39460	<0.02
ICAM-1	2.42539	2.31482	<0.03
NO SIGNIFICANT VARIABLES	β	T	p
sRAGE	0.39173	1.41420	0.2
HOMA-IR	0.18898	1.22232	0.2
Rigidity index	-0.16816	-1.21967	0.2
Age	-0.22614	-0.92035	0.4
NORMAL WEIGHT GROUP			
SIGNIFICANT VARIABLES	β	T	p
Carotid intima media thickness (CIMT)	-0.489868	-6.75648	<0.00001
HOMA-IR	0.434311	4.30263	<0.0001
Ankle branchial index (AAI)	0.186815	2.99637	<0.005
sRAGE	0.298611	2.75265	<0.001
LDL-C	0.133326	2.14750	<0.04
NO SIGNIFICANT VARIABLES	β	T	P
8-oxo-dG	-0.182463	-1.89383	0.07
Dietary AGES	0.100727	1.69514	0.1
HDL-C	-0.089001	-1.24935	0.2

Table 3
Factors associated with CML

TOTAL GROUP			
SIGNIFICANT VARIABLES	β	T	P
ICAM-1	0.481575	3.85074	<0.0001
HOMA-IR	0.318877	2.60826	<0.01
Rigidity index	0.219508	2.47079	<0.01
Age	-0.191664	-2.36497	<0.02
Carotid intima media thickness (CIMT)	-0.169359	-1.99073	<0.05
NO SIGNIFICANT VARIABLES	β	T	P
Skin autofluorescence	-0.157728	-1.57709	0.1
Ankle branchial index (AAI)	0.120363	1.34975	0.2
Triglycerides	0.092195	1.17181	0.3
OBESE GROUP			
SIGNIFICANT VARIABLES	B	T	p
HOMA-IR	0.601326	3.67495	<0.0001
HbA1C	-0.394868	-2.65039	<0.01
AGE	-0.271779	-2.43681	<0.02
Rigidity index	0.257712	2.22460	<0.03
LDL-C	-0.290782	-2.27341	<0.03
NO SIGNIFICANT VARIABLES	β	T	p
HDL-C	0.220404	1.94086	0.06
Carotid intima media thickness (CIMT)	-0.145796	-1.38807	0.2
sRAGE	0.173653	1.04665	0.3
NORMAL WEIGHT GROUP			
SIGNIFICANT VARIABLES	β	T	p
Flow-mediated dilation in the brachial artery (FMD)	-0.477419	-3.28308	<0.002
HbA1C	0.290606	2.05746	<0.05
NO SIGNIFICANT VARIABLES	β	T	p
Age	-0.221917	-1.67251	0.1

Graphic 2
Correlation between serum CML levels and ICAM-1 levels in the Total Group



Graphic 1
Correlation between Skin autofluorescence and cIMT in the Total Group

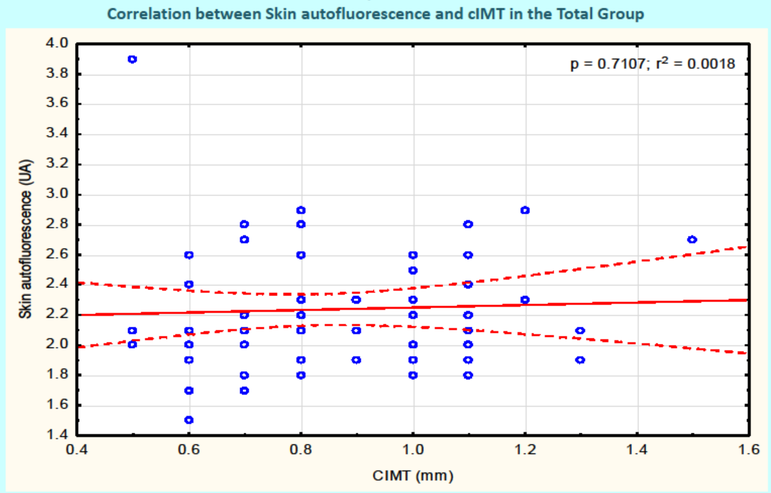


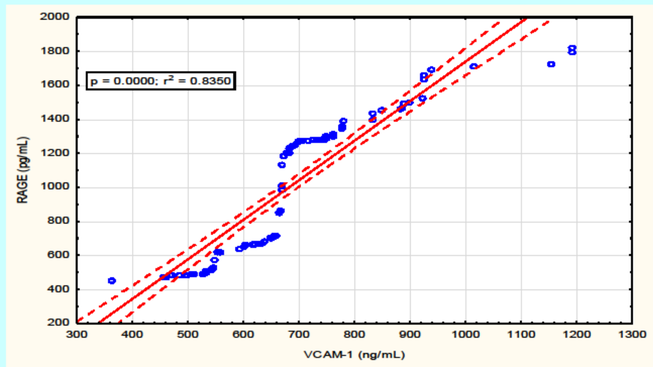
Table 3
Factors associated with sRAGE

TOTAL GROUP			
SIGNIFICANT VARIABLES	β	T	p
VCAM-1	0.712996	3.74441	<0.0001
Carotid intima media thickness (CIMT)	0.159989	3.29931	<0.001
Skin autofluorescence	0.145904	2.90850	<0.005
MDA	0.782332	2.94545	<0.004
ICAM-1	-0.653035	-2.69920	<0.009
Framingham Risk Score	-0.174430	-2.24291	<0.03
NO SIGNIFICANT VARIABLES	β	T	p
LDL-C	0.413738	1.95849	0.05
Rigidity index	0.098117	1.49039	0.1
Dietary AGES	0.063309	1.52494	0.1
8-oxo-dG	-0.175297	-1.21979	0.2
Flow-mediated dilation in the brachial artery (FMD)	-0.080861	-1.16806	0.2
Cholesterol	-0.340857	-1.50225	0.1
Age	0.104265	1.43896	0.2
Triglycerides	0.110423	1.07545	0.3
OBESE GROUP			
VARIABLE SIGNIFICATIVAS	β	T	p
MDA	1.74517	4.42309	<0.0001
8-oxo-dG	-2.26925	-5.08818	<0.00001
Rigidity index	0.16328	2.90950	<0.007
VCAM-1	0.72670	2.48130	<0.019
HbA1C	-0.12916	-2.39186	<0.023
NO VARIABLE SIGNIFICATIVAS	β	T	p
ICAM-1	0.53544	1.52254	0.1
Dietary AGES	0.09981	1.74828	0.09
Ankle branchial index (AAI)	-0.12488	-1.89588	0.07
Carotid intima media thickness (CIMT)	0.09079	1.69182	0.1
BMI	-0.05297	-1.01500	0.3

Table 4
Factors associated with sRAGE

NORMAL WEIGHT GROUP			
VARIABLES SIGNIFICATIVAS	β	T	p
MDA	1.495045	7.00776	<0.001
ICAM-1	-0.746661	-3.58571	<0.001
8-oxo-dG	0.164244	2.30860	<0.03
Rigidity index	0.111772	2.24687	<0.03

Graphic 3
Correlation between serum sRAGE levels and VCAM-1 levels in the Total Group



Conclusion

The results show association of serum AGEs with ICAM-1 and HOMA-IR and strong association of sRAGE with VCAM-1, ICAM-1, MDA and cIMT.

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