RELATIONSHIP BETWEEN SERUM 25-HYDROXIVITAMIN D3 AND ADIPOSE TISSUE VITAMIN D RECEPTOR (VDR) GENE EXPRESSION WITH OBESITY AND TYPE 2 DIABETES

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INTRODUCTION:

25-hydroxyvitamin D (25(OH)D3) deficiency has been associated with diabetes and obesity. However, the mechanisms underlying these relationships are not completely understood.

Vitamin D receptor (VDR) is expressed in adipose tissue; it has been reported a higher expression in obese patients than in lean subjects, suggesting a differential vitamin D dynamics in adipose tissue according to the obesity degree. In addition, 1, 25-dihydroxyvitamin D3 (1,25(OH)2D3) is able to modify VDR gene expression in mice 3T3-L1 preadipocytes.

OBJETIVE:

To analyze plasma 25(OH)D3 and VDR gene expression in adipose tissue according to body mass index (BMI) and glycemic status.

To evaluate the influence of 1,25(OH)2D3 and VDR gene expression in human adipose tissue cultures.

MATHERIALS AND METHODS:

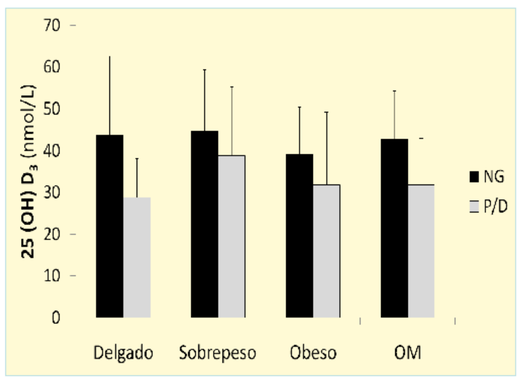
We recruited and classified 119 subjects according to their BMI (lean, overweight, obese and morbidly obese subjects) and to their glycemic status: normoglycemic (NG) and prediabetic/diabetic (P/D) patients. We measure plasma 25(OH)D3 and parathyroid hormone (PTH) levels as well as VDR gene expression in visceral adipose tissue. Adipose tissue from morbidly obese (ATMO) and lean (ATL) donors were cultured and treated with a range of 1,25(OH)2D3 concentrations.

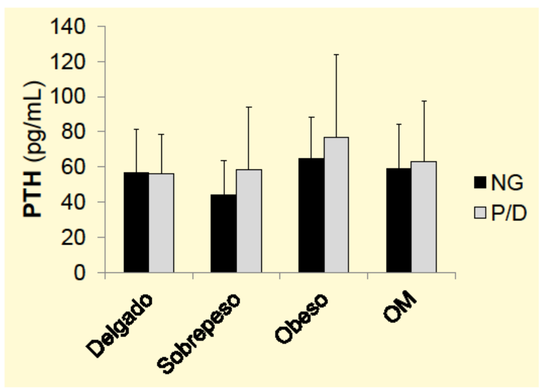
RESULTS:

Table 1. Anthropometric and biochemicals characteristics of the study groups:

	Lean		Overweight		Obese		Morbidly obese	
	NG (n=15)	**P/D** (n=16)	**NG** (n=18)	**P/D**(n=13)	**NG** (n=13)	**P/D** (n=16)	**NG** (n=12)	**P/D** (n=15)
Age (years)	47.0±14.0^{a,b}	53.7±15.9^{b,c,d}	47.8±12.7^{a,b,c}	58.1±10.9^{c,d}	52.1±16.9^{b,c}	63.0±13.9^{d}	40.2±8.5^{a}	38.4±10.5^{a}
% ♂/ ♀	60/40	62.5/37.5	55.6/44.4	53.8/46.2	46.2/53.8	37.5/62.5	50/50	40/60
BMI (Kg/m^2)	23.8±1.2^{a}	24.1±1.1^{a}	27.6±1.4^{b}	27.2±1.2^{b}	33.6±3.2^{c}	33.5±3.1^{c}	50.6±6.7^{d}	51.1±5.6^{d}
Waist (cm)	83.9±7.9 ^{a}	90.1±7.6 ^{a,b}	92.1±4.9 ^{a,b}	95.1±8.1 ^{b}	108.2±9.1 ^{c}	107.2±10.8^{c}	132.7±14.2^{d}	144.4±19.0^{e}
Insulin(µUI/mL)	8.2±2.3^{a}	11.6±8.0^{a,b}	7.4±3.7^{a}	11.2±5.6^{a,b}	8.5±3.1^{a}	15.4±6.4^{b}	12.3±5.4^{a,b}	28.8±17.5 ^{c}
Glucose(mg/dL)	84.0±10.2^{a}	108.1±7.1^{b}	89.9±12.3^{a}	125.3±18.8^{c}	90.2±5.0^{a}	128.6±37.4^{c}	88.6±6.3^{a}	123.9±34.0^{c}
HOMA-IR	1.7±0.5^{a}	3.1±2.1^{a,b}	1.6±0.9^{a}	3.5±2.2^{b,c}	1.9±0.7^{a,b}	4.8±2.0^{c}	2.7±1.0^{a,b}	8.5±4.6 ^{d}
Col (mg/dL)	200.1±37.7^{a,b,c}	214.2±29.8^{a,b}	193.2±28.5^{b,c}	224.4±34.0^{a}	200.3±40.3^{a,b,c}	224.6±47.8^{a}	179.5±36.6^{c}	191.3±29.0^{b,c}
TG (mg/dL)	95.6±40.9^{a}	158.5±91.9^{b}	103.1±42.2^{a}	139.0±48.4^{a,b}	120.5±43.6^{a,b}	155.2±65.4^{b}	122.4±56.2^{a,b}	142.9±44.8^{a,b}
HDL-C (mg/dL)	54.7±16.4^{a}	49.3±12.0^{a}	53.4±11.6^{a}	51.5±15.9^{a}	55.0±6.8^{a}	53.7±15.8^{a}	45.6±10.9^{a}	45.0±11.4^{a}
TAS (mmHg)	124.0±14.2^{a}	129.1±19.3^{a,b}	126.2±14.6^{a,b}	133.4±22.4^{a,b}	127.5±21.9^{a,b}	141.5±22.2^{b}	129.0±21.6^{a,b}	137.5±17.9^{a,b}
TAD (mmHg)	73.9±9.5^{a}	76.6±11.7^{a}	75.2±12.6^{a}	80.8±10.4^{a}	79.6±13.3^{a}	81.8±10.6^{a}	83.3±10.78^{a}	80.9±8.9^{a}

Values are presented as mean ± SD. Different letters indicate significant differences between groups ($p < 0.05$). BMI, body mass index; HOMA-IR index of insulin resistance; Col Cholesterol; TG, triglycerides; TAS, Systolic Blood Pressure; DBP, diastolic blood pressure.





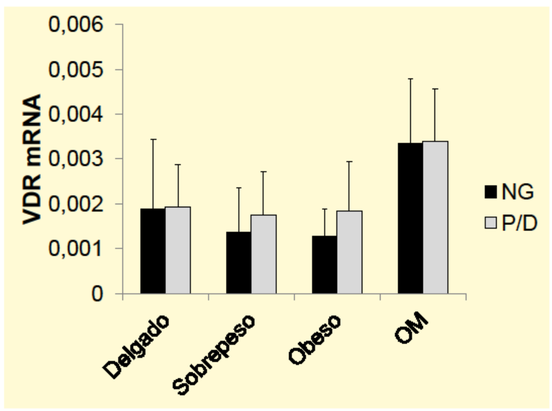
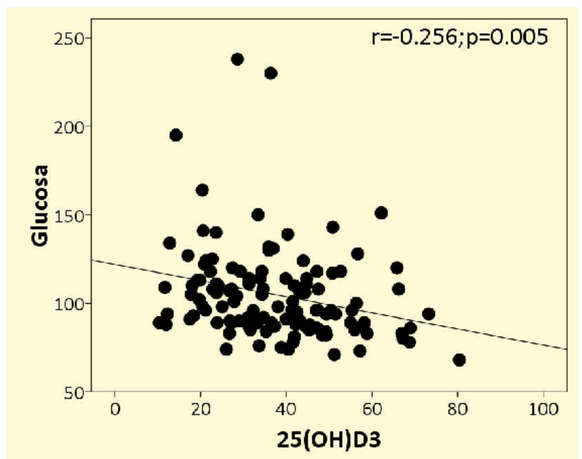
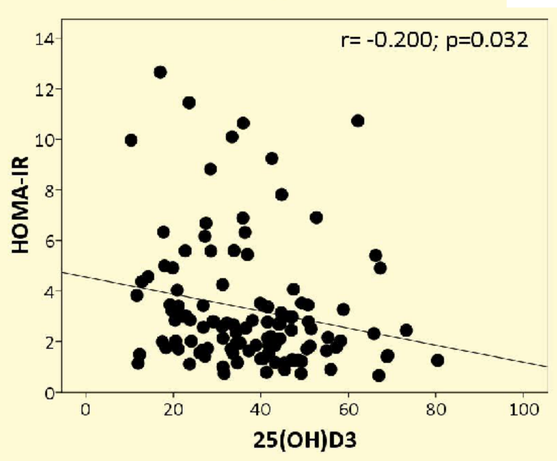


Figure 1. Plasma levels of 25 (OH) D3 and PTH in the study groups. Gene expression levels in adipose tissue VDR.





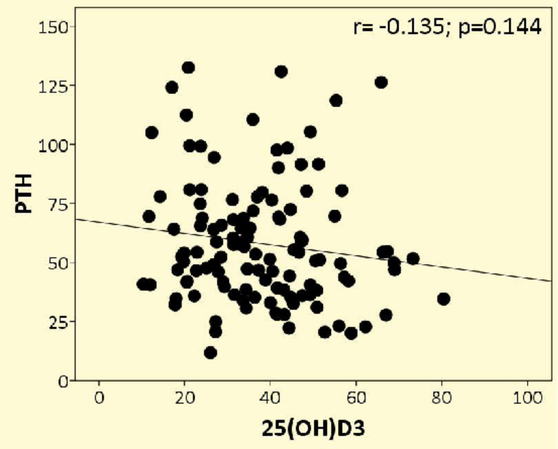


Figure 2. Correlation of plasma levels of 25 (OH) D3 with HOMA-IR, blood glucose levels and PTH.

CONCLUSIONS:

Plasma 25(OH)D3 are diminished in P/D patients compared to NG subjects independently of BMI and are closely related with glucose metabolism variables, suggesting that vitamin D deficiency is associated more with carbohydrate metabolism than with obesity.

Adipose tissue VDR gene expression was significantly higher in morbidly obese patients than in the other BMI groups and its regulation by 1,25(OH)2D3 was only demostrated in morbidly obese subjects.

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Calcium, vitamin D and bone

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