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CORRELATIONS OF SERUM VITAMIN D WITH METABOLIC PARAMETERS IN ADULT OUTPATIENTS WITH DIFFERENT DEGREES OF OVERWEIGHT / OBESITY COMING FROM AN URBAN COMMUNITY

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Abstract

Objective. To describe the correlations between serum 25(OH) vitamin D and anthropometric and metabolic parameters in adult outpatients of both sexes with different BMI coming from an urban community.

Subjects and Methods. 264 subjects referred for obesity assessment participated – 109 men and 155 women (20-60 years). Body weight and height, waist circumference (WC), blood pressure were recorded. Body composition was assessed by bioelectrical impedance (BIA) on a Tanita BC 420 MA analyzer (Tanita Inc., Japan). Serum 25(OH)D Total, Insulin, High-sensitivity C-reactive protein, blood glucose, total, HDL-cholesterol and triglycerides were measured. The insulin resistance index was calculated (HOMA-IR). Participants with BMI>25.0 kg/m^2 underwent standard 75 g OGTT. Statistical analysis was performed on an IBM SPSS Statistics 19.0 for Windows platform (Chicago, IL).

Results. Normal weight was found in 27.2 % of the participants, 24.6 % had overweight, 29.2 % -class I obesity, and 18.9 % – class II or III. Vitamin D was weakly and inversely correlated to different variables in the whole group – such as weight, WC, WC/Height, % body fat and HOMA-IR index (r=-0.231, -0.283, -0.307, -0.339, -0.328 respectively, all p<0.001). Building subgroups based on BMI led to loss of significance. Backward analysis revealed Total-C/LDL-C ratio, and LDL-C/HDL-C ratio as strongest predictors of serum vitamin D (p=0.001; R2=0.204).

Conclusion. The association of vitamin D with blood pressure, plasma lipids, glucose and insulin is very weak on an individual level. However, several obesity indices (WC, WC/height ratio, % Body fat from BIA) might be used as a screening tool for subjects at risk for vitamin D deficiency.

Key words: body composition, obesity, metabolism parameters, vitamin D.

INTRODUCTION

Vitamin D insufficiency and deficiency have become a global health problem during the past decade (1, 2). Traditionally they were linked to low bone density, osteoporosis and fracture risk (3, 4). However, the relationship between the vitamin D status and different features of the metabolic syndrome and the related cardiovascular risk has come increasingly into focus. The negative correlations of serum vitamin D levels with different metabolic parameters have been extensively studied. There are a number of publications correlating serum 25(OH)D levels with serum lipids (5-7), blood pressure (8, 9), glycemic control or insulin resistance (10-15). Their results are however varying and even conflicting. As an example, a cross-sectional study reported that vitamin D was a significant independent inverse determinant of total cholesterol, LDL-C and triglycerides in hyperlipidemic patients (6), while another one described separate associations for men and women (5). A cross-sectional study found higher vitamin D levels in patients with systolic blood pressure (SBP) above 130 mm Hg as compared with patients with SBP lower than 130 mm Hg (8), while a randomization analysis including genetic data proved the opposite (9). A study in postmenopausal women did not find an association of vitamin D with blood glucose levels (10), another one identified a threshold effect of 25(OH)D on glucose–insulin metabolism (12). Poor vitamin D status had been associated with insulin resistance in nondiabetic obese patients (15). Several of the published cross-sectional and interventional studies (with vitamin D supplementation) were focused on specific aspects of the metabolic syndrome such as lipids (16,17), obesity (18-20), blood pressure (21-23),

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insulin resistance or glycemic control (24-26). Very few of them correlated serum vitamin D levels with data from oral glucose tolerance tests (25) or combined laboratory metabolic data with bio-electrical body impedance analysis (BIA) (27).

The aim of the present study was to describe the correlations of serum 25(OH)D levels with a complex of anthropometric and metabolic parameters in men and women with different BMI and to add data from BIA and OGTT (the latter in those with obesity).

SUBJECTS AND METHODS

Subjects

This is a cross-sectional observational study. It was approved by the responsible ethical authorities and was in compliance with ethical standards and the Declaration of Helsinki. Each participant signed informed consent prior to any procedure. The participants came from the general population in an urban community. They were referred to by their GPs to a medical practice specialized in diet counselling and weight management. The inclusion criteria were age between 18 and 60 years and willingness to participate. The age range was selected to avoid the additional confounding influence on body composition of age-related sarcopenia. The exclusion criteria were severe or chronic diseases or medications known to affect body weight, immobilization, and others known to induce morbid obesity. Among the exclusion criteria were conditions such as heart failure NYHA III and IV, respiratory failure, chronic kidney disease stage III to V, liver cirrhosis, pancreatitis, musculoskeletal disorders (severe fractures, disability) etc. Among the medications that were not allowed were glucocorticoids, immunosuppressive drugs, antipsychotic drugs, vitamins (especially vitamin D) and others.

Five hundred outpatients were offered to participate in this study and 264 consented – 109 men (41.3 %) and 155 (58.9 %) women.

Methods

Medical history was collected and anthropometric measurements were performed. Body weight was measured by a calibrated digital scale (Tanita BC 420 MA, Tanita Inc., Japan) to the nearest 0.1 kg in light clothes without shoes. Body height was recorded in the upright position without shoes to the nearest 0.5 cm. BMI was calculated in kg/m^2. The waist circumference (WC) was measured in the upright position in the horizontal plane above the iliac crest by a tape to the nearest 0.5 cm. The visceral obesity was defined as WC > 80 cm for women and > 94 cm for men. The waist to height ratio (W/H ratio) was computed with the reference range below 0.5 for both sexes. Blood pressure was measured twice by an aneroid sphygmomanometer in the sitting position after 15 minutes of rest and the average value was recorded. Body composition was recorded by a leg-to-leg 50 kHz bioelectrical impedance analyzer (Tanita BC 420 MA, Tanita Inc., Japan) according to the instructions of the manufacturer and the predictive formula incorporated in this device. The accuracy error at first calibration is ± 2% for the impedance measurement and ± 0.2 kg for body weight (28).

The blood samples were taken between 8:00 and 10:00 a.m. after an overnight fasting. Routine blood biochemistry (total cholesterol and HDL direct, triglycerides) was performed on a Cobas Integra 400+ analyzer. Fasting plasma glucose was determined by the hexokinase method. Additionally, the ratios of LDL-cholesterol to HDL-cholesterol were calculated.

Serum 25-(OH)-Vitamin D and insulin were measured by electro-chemi-luminescent detection (ECLIA method on an Elecsys 2010 analyzer, Roche Diagnostics, Switzerland). The intra-assay error for 25(OH)D assessed as coefficients of variation (CV%) is 1.7 – 7.8%, the correlation with liquid chromatography/ mass spectrometry (LC-MS/MS) is characterized by Pearson's r = 0.894. The intra-assay error for serum insulin as described by the manufacturer was CV% 1.7 – 1.9%. High-sensitivity cardiac C-reactive protein was measured by an immune-turbo-dimetrical method on a Cobas Integra 400+ analyzer.

Subjects with serum 25(OH)D < 25.0 nmol/L were defined as deficient, those with levels between 25.0 and 49.9 nmol/L – as insufficient and ≥ 50 nmol/L as sufficient (3). Levels ≥ 75.0 nmol/L were defined as optimal for bone health. Bearing in mind the seasonal variations in serum vitamin D levels, the recruitment period was for 2 years from November till May to include individuals during lowest sunshine.

Insulin resistance was calculated as HOMA-IR - from fasting plasma glucose (in mmol/L) multiplied by plasma insulin (in IU/L) and divided by 22.5.

All patients with BMI >25.0 kg/m^2 underwent the standard 75 g Oral Glucose Tolerance Test (OGTT) on a separate morning visit after an overnight fasting with blood samples collected for blood glucose (FPG) and Insulin at baseline, 1st and 2nd hour post-challenge (60' and 120').

Statistical analysis

Statistical analyses were done using the SPSS 23.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics and variation analysis were first performed. A normal distribution was tested by the Shapiro-Wilk and Kolmogorov-Smirnov tests. Descriptive statistics were compared between groups via the Mann-Whitney and Cruscal-Wallis tests for continuous variables and via the Fisher's exact and $\chi 2$ tests – for categorical variables. Data were analyzed according to sex and BMI categories. ANOVA, correlation, univariate and multiple linear regression analyses were performed. The step-wise backward procedure was applied to determine predictive factors in the multivariate analysis. Vitamin D was inserted in the analyses as the dependent variable. The vitamin D levels had not a Gaussian distribution; therefore, in the regression analyses it was corrected by root extraction. Obesity grades II and III were merged to increase the number of participants in the subgroup of high-grade obesity. Statistical significance was set as $p \leq 0.05$; all tests were two-tailed.

RESULTS

The mean age of the 264 participants (155 women, 109 men) was 41.2 ± 10.5 years. Their age distribution was as follows: 20-29 years – 13 men and 24 women; 30-39 years – 34 M and 47 F, 40-49 years – 44 M and 40 F; 50-59 years – 18 M and 44 F.

Participants' characteristics in the group as a whole and according to sex and BMI

Normal BMI was found in 72 (27.2%) of the participants, 65 (24.6%) had overweight, 77 (29.2%) had obesity grade I and the remaining 50 (18.9%) – obesity grade II or III. Normal WC was found in 18.9% of the participants and normal WC/height ratio - in 22.3%. The SBP exceeded 140 mm Hg in 23.5% of the participants, the DBP exceeded 90 mm Hg in 29.5%. The % BF was above the upper reference range in 30.7% of the participants. Normal fasting glycemia was registered in 77.3% of the subjects (below 5.6 mmol/L in 56.8%; and between 5.6 and 6.0 mmol/L – in 20.5%), 14.8% had impaired fasting glycemia (FPG between 6.1 and 6.9 mmol/L), while 8.0% had type 2 diabetes (FPG above 7.0 mmol/L). Total cholesterol was < 5.0 mmol/L in 47.3% of the study population; and it was above 6.1 mmol/L in 15.9%. The LDL-C was < 2.6 mmol/L in only 29.3%, and it was between 2.6 and 4.1 mmol/L in 59.0%. The HDL-C was low (<1.0 mmol/L in men and <1.2 mmol/L in women) in 25.2%, while the triglycerides were elevated (>1.7 mmol/L) in 20.5%. Fasting plasma insulin of 43.5% of the participants exceeded 25 mUI/L, and the HOMA-IR index was above 2.5 in 42.5%, while the hs-CRP exceeded 5 mg/L in 30.5%.

The anthropometric, body composition and laboratory data of the participants are summarized in Table 1 according to sex. Men and women differ significantly in most baseline parameters except for age and total-C. Women had higher levels of LDL-C and % BF than men.

The anthropometric, body composition and laboratory data of the participants are summarized in Table 2 according to BMI. The FPG and LDL-C were lower in subjects with normal BMI, but the differences across higher BMI categories did not reach significance. SBP, DBP, triglycerides, HDL-C and both ratios LDL-C/HDL-C and Total-C/HDL-C differed significantly in subjects with normal BMI, overweight and obesity; however, the differences across the different classes of obesity were not significant.

Correlation analysis of serum vitamin D with the anthropometric and metabolic parameters according to age and sex

The Spearman's correlation coefficients relating the vitamin D levels to the anthropometric and metabolic parameters are shown in Table 3 in the group as a whole and in men and women separately. Vitamin D was inversely and weakly correlated to most of the parameters except for LDL-C. In men fewer parameters were correlated to vitamin D with SBP, LDL-C/HDL-C and hs-CRP being no more associated. In women the DBP and the FPG were no more associated with the vitamin D levels.

The Spearman's correlation coefficients relating the vitamin D levels and the anthropometric and metabolic parameters are shown in Table 4 according to the BMI category. By dividing the whole study group in 4 BMI categories most of the variables lost their associations with the vitamin D levels. In overweight individuals serum vitamin D correlated only with the WC and the WC/Height ratio, while in class I obesity the correlation with the WC remained as the only significant one. In obesity class II+ more variables were moderately and inversely correlated to vitamin D: % BF, Triglycerides, LDL-C/HDL-C ratio, HOMA-IR index, hs-CRP. The correlation of vitamin D with the 2hr OGTT glucose level was strong and inverse.

Table 1. The descriptive statistics of the participants are shown according to sex

	Total (N = 264)			**Men (N = 109)**		**Women (N = 155)**	
Variable	Mean	SD	Min - Max	Mean	SD	Mean	SD
Age (years)*	41.2	10.5	19.0 - 60.0	40.6	9.6	41.6	11.1
Weight (kg)*	87.3	22.7	45.7 - 174.0	101.6	19.7	77.2	18.9
Height (cm)*	170.7	8.9	150.0 - 194.0	178.3	6.5	165.4	6.0
BMI (kg/m^2)*	29.77	6.68	18.54 - 53.66	31.97	6.03	28.22	6.70
WC (cm)*	99.9	16.5	66.0 - 146.0	108.6	15.0	93.8	14.7
% FM (%)*	32.9	9.4	14.5 - 55.3	28.4	7.6	36.1	9.3
SBP (mmHg)*	124.5	19.0	70- 190	132.5	14.7	118.8	19.7
DBP (mmHg)*	81.8	11.8	50 - 120	87.0	9.1	78.1	12.2
Serum 25(OH) D (nmol/L)	38.15	22.84	7.48 – 129.2	39.25	21.95	37.38	23.49
Fasting glucose (mmol/L) *	6.07	2.94	1.81 - 17.60	5.99	1.45	5.38	0.73
T-Chol (mmol/l)	5.63	1.13	3.41 - 14.70	5.17	1.00	5.20	0.97
Triglycerides (mmol/L)*	1.24	0.81	0.23 - 3.84	1.53	0.89	1.06	0.70
LDL-C (mmol/L)*	1.35	1.43	0.23 - 15.24	3.33	0.90	3.00	0.94
HDL-C (mmol/L) *	3.13	0.93	0.40 - 5.80	1.17	0.30	1.64	0.51
LDL-C/HDL-C *	1.45	0.50	0.71 - 3.00	3.02	1.09	2.09	1.09
T-CHOL /HDL-C *	2.46	1.18	0.16 - 6.85	4.73	1.43	3.47	1.36
Insulin (mIU/L) $_a$ *	10.92	8.34	0.58 - 56.04	12.96	10.02	9.16	6.13
HOMA–IR index $_a$ *	2.75	2.02	0.10 - 9.82	3.24	2.22	2.35	1.76
OGTT Insulin 60' (μIU/mL) $_b$	65.45	42.80	2.34 - 159.50	77.90	43.87	56.88	41.23
OGTT Insulin 120' (μIU/mL) $_b$	26.57	16.22	4.91 - 53.89	20.44	16.20	30.25	15.61
OGTT Glucose 60' (mmol/L) $_b$	8.60	3.09	3.95 - 16.46	8.25	2.76	8.81	3.32
OGTT Glucose 120' (mmol/L) $_b$	5.76	1.31	3.23 - 8.10	5.48	1.44	5.94	1.23
hs CRP (mg/L)	4.03	3.71	0.21 - 17.68	3.48	3.10	4.63	4.22

* p<0.001 for the difference between men and women. $_a$ basal values for the whole study group. $_b$ values during the OGTT which was performed only in subjects with BMI ≥ 25.0 kg/m^2.

Table 2. The descriptive statistics of the participants according to their BMI is shown. Obesity grade II and III are merged

	Normal BMI (N = 72)		**Overweight (N = 65)**		**Obesity class I (N =77)**		**Obesity class II-III (N = 50)**	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	34.3 $_a$	9.8	**43.8** $_b$	8.9	**44.2** $_b$	10.6	**43.0** $_b$	8.9
Weight (kg)	63.4 $_a$	10.1	80.1 $_b$	9.1	95.7 $_c$	12.5	**118.0** $_d$	16.9
Height (cm)	169.8 $_a$	7.9	169.3 $_a$	8.4	171.8 $_a$	9.9	172.2 $_a$	8.9
BMI (kg/m^2)	21.86 $_a$	2.11	27.86 $_b$	1.26	32.30 $_c$	1.49	**39.73** $_d$	4.42
WC (cm)	81.7 $_a$	7.5	95.7 $_b$	8.4	106.0 $_c$	7.9	**122.1** $_d$	10.6
WC/Height	0.48 $_a$	0.04	0.57 $_b$	0.05	0.62 $_c$	0.05	**0.71** $_d$	0.06
SBP (mmHg)	109.6 $_a$	15.7	122.2 $_b$	14.6	**133.0** $_c$	17.1	**135.7** $_c$	16.7
DBP (mmHg)	72.0 $_a$	9.5	80.3 $_b$	8.4	**86.7** $_c$	10.0	**90.2** $_c$	10.9
% FM (%)	23.4 $_a$	6.2	33.0 $_b$	6.8	35.7 $_c$	7.2	**42.2** $_d$	7.0
Serum 25(OH) D (nmol/L)	48.80 $_a$	25.91	37.82 $_b$	21.10	35.62 $_b$	21.41	27.15 $_c$	15.35
Fasting glucose (mmol/L)	5.06 $_a$	0.61	**5.65** $_b$	0.70	**5.82** $_b$	1.15	**6.14** $_b$	1.67
T-Chol (mmol/L)	4.99 $_a$	0.86	5.08 $_{ac}$	0.98	5.40 $_{bc}$	1.06	5.28 $_a$	0.98
Triglycerides (mmol/L)	0.72 ^{a}	0.47	1.17 ^{b}	0.56	**1.66** ^{c}	0.93	**1.70** ^{c}	0.89
LDL-C (mmol/L)	2.71 $_a$	0.94	**3.17** $_b$	0.80	**3.35** $_b$	0.98	**3.48** $_b$	0.81
HDL-C (mmol/L)	**1.89** $_a$	0.50	1.37 $_b$	0.36	1.19 $_c$	0.33	1.18 $_c$	0.30
LDL-C / HDL-C	1.61 $_a$	0.93	2.47 $_b$	0.87	**3.00** $_c$	1.14	**3.16** $_c$	1.15
T-Chol/HDL-C	2.84 $_a$	1.05	3.94 $_b$	1.10	**4.83** $_c$	1.45	**4.83** $_c$	1.53
Plasma insulin (μIU/mL)	5.23	2.41	8.58	6.96	10.58	6.75	18.86	23.93
HOMA-IR index	1.14	0.69	2.32	2.35	2.99	2.31	5.83	9.76

The same upper-case letter in the horizontal line represents no significant difference, while different letters suggest significant differences between BMI subgroups (p≤0.05). The bold letters highlight the presence of statistical significance.

Table 3. The Spearman's correlation coefficients between serum 25(OH)D and the anthropometric and metabolic parameters are shown according to sex

Independent variable	Total group (N=264)	Men (n=109)	Women (n=155)
Age (years)	-0.077	-0.065	-0.072
Weight (kg)	-0.231 $_{c}$	-0.279 $_{b}$	-0.330 $_{c}$
Height (cm)	0.052	0.065	-0.070
WC (cm)	-0.283 $_{c}$	-0.393 $_{c}$	-0.299 $_{c}$
WC/Height	-0.307 $_{c}$	-0.384 $_{c}$	-0.286 $_{c}$
SBP (mmHg)	-0.159 $_{b}$	-0.172	-0.212 $_{b}$
DBP (mmHg)	-0.138 $_{a}$	-0.204 $_{a}$	-0.145
% Body fat	-0.339 $_{c}$	-0.393 $_{c}$	-0.316 $_{c}$
Fasting glucose (mmol/L)	-0.149 $_{a}$	-0.296 $_{b}$	-0.089
T-Chol (mmol/L)	0.017	-0.052	0.063
Triglycerides (mmol/L)	-0.232 $_{b}$	-0.385 $_{c}$	-0.184 $_{a}$
LDL-C (mmol/L)	0.215 $_{b}$	0.271 $_{a}$	0.310 $_{c}$
HDL-C (mmolL)	-0.084	-0.038	-0.124
LDL-C / HDL-C ratio	-0.183 $_{b}$	-0.205	-0.259 $_{b}$
T-CHOL /HDL-C ratio	-0.190 $_{b}$	-0.258 $_{a}$	-0.256 $_{b}$
Insulin (mUI/L)	-0.281 $_{b}$	-0.282 $_{a}$	-0.286 $_{a}$
HOMA – IR index	-0.328 $_{c}$	-0.433 $_{b}$	-0.269 $_{a}$
hs CRP (mg/L)	-0.293 $_{b}$	-0.230 $_{a}$	-0.300 $_{a}$
OGTT Insulin 60' (μIU/mL)	0.105	-0.091	0.180
OGTT Insulin 120' (μIU/mL)	-0.279	-0.600	0.061
OGTT Glucose 60' (mmol/L)	-0.251	-0.358	-0.079
OGTT Glucose 120' (mmol/L)	-0.334	-0.636 ^{a}	-0.121

$_{a}$ p<0.05, $_{b}$ p<0.01, $_{c}$ p<0.001.

Table 4. The Spearman's correlation coefficients between serum 25(OH)D and the anthropometric and body composition parameters are shown according to BMI

Independent variable	Normal weight	Overweight	Obesity I degree	Obesity II+ degree
Age (years)	0.209	-0.005	-0.122	0.214
Weight (kg)	0.029	0.116	0.120	-0.114
Height (cm)	0.079	0.022	0.143	0.078
WC (cm)	-0.179	0.265 $_{a}$	-0.107	-0.139
WC/Height	-0.233 $_{a}$	0.298 $_{a}$	-0.278 $_{a}$	-0.257
SBP (mmHg)	0.002	0.070	-0.079	-0.014
DBP (mmHg)	0.027	0.171	-0.093	-0.007
% FM (%)	-0.146	-0.101	-0.216	-0.303 $_{a}$
Fasting glucose (mmol/L)	0.102	0.000	-0.158	-0.035
T-Chol (mmol/L)	0.250 $_{a}$	-0.073	0.062	-0.067
Triglycerides (mmol/L)	-0.020	0.144	-0.026	-0.378 $_{a}$
LDL-C (mmol/L)	0.129	-0.103	-0.073	0.260
HDL-C (mmol/L)	0.158	-0.033	0.136	-0.190
LDL-C / HDL-C ratio	0.025	0.047	0.158	-0.309 $_{a}$
T-CHOL /HDL-C ratio	-0.008	0.086	0.150	-0.226
Fasting insulin (mIU/L)	0.886 $_{a}$	-0.137	-0.178	-0.251
HOMA – IR index	0.886 $_{a}$	-0.169	-0.213	-0.366 $_{a}$
hs CRP (mg/L)	NA	-0.037	-0.023	-0.378 $_{a}$
OGTT Insulin 60' (μIU /mL)	NA	0.547	-0.143	0.024
OGTT Insulin 120' (μIU /mL)	NA	-0.082	-0.321	-0.486
OGTT Glucose 60' (mmol/L)	NA	0.410	-0.690	-0.500
OGTT Glucose 120' (mmol/L)	NA	-0.196	-0.357	-0.786 $_{a}$

$_{a}$ p<0.05.

Prediction models from the regression analysis

The primary regression analysis included all variables and attained an adjusted coefficient R2=0.125, p=0.099 (see Table 5). The highest predictive power was attributed to body weight, followed by FM (in kg) and BMI (in kg/m^2). This primary model did not reach statistical significance and a strong co-linearity

Table 5. The regression coefficients in the final multiple backward linear regression analysis are shown

Predictors	Non-standardized coefficients		Standardized coefficients	P
	B	Std. Error	Beta	
Total-C / LDL-C ratio	0.987	0.357	1.045	0.007
LDL-C / HDL-C ratio	-0.984	0.395	-0.771	0.015
HDL-C (mmol/L)	1.609	0.639	0.389	0.014
Triglycerides (mmol/L)	-0.540	0.269	-0.304	0.049
FM (%)	-0.040	0.018	-0.243	0.035
SBP (mmHg)	-0.016	0.009	-0.209	0.069
Constant	5.881	1.669		0.001

was present. The Backward analysis attained statistical significance (p=0.001; R2=0.204) with Total-C/ LDL-C ratio, and LDL-C/HDL-C ratio being the strongest predictors. The relationship of vitamin D with all the predictors was negative except for Total-C and HDL-C. Adjusting for age, sex or BMI did not improve the significance of the data and did not bring additional information.

Additional findings

As an additional finding we were able to prove a weak negative correlation of serum vitamin D with hs-CRP and % body fat in the population as a whole as well as in men and women separately. Both markers remained significantly related to vitamin D in the obese population (grade II-III) even after adjusting for BMI.

DISCUSSION

In this cross-sectional observational study we examined the correlations of serum 25(OH) vitamin D levels with anthropometric and metabolic parameters (lipids, glycemia and BP). We were able to prove significant correlations of vitamin D with serum triglycerides, LDL-C, fasting plasma insulin, the HOMA-IR and hs-CRP, as well as with the SBP. There were also correlations with lipid ratios (Total-C/ HDL-C; LDL-C / HDL-C) as well as a weaker one with DBP. The blood glucose and plasma insulin in the course of OGTT were not correlated to the vitamin D status. Building subgroups according to the BMI categories led to loss of statistical significance. In a multivariate model the lipids remained to be the best predictors of the vitamin D levels.

Serum vitamin D and lipids

The relationship between vitamin D deficiency and lipids was acknowledged by a number of cross-sectional studies in large population samples. In a Norwegian study combining cross-sectional and longitudinal data there was a significant increase in serum Total Cholesterol (TC), HDL-C and LDL-C, and a significant decrease in serum LDL-C/HDL-C ratio and triacylglycerol across increasing serum 25(OH)D quartiles (17). In a Chinese study the serum 25(OH)D levels were inversely associated with the triglycerides (β coefficient = -0.24) and LDL-C (β coefficient = -0.34) and positively associated with Total Cholesterol, TC (β coefficient = 0.35) in men; while in women the strongest associations were with serum 25(OH)D and LDL-C (β coefficient = -0.25) and TC (β coefficient = 0.39) (5). These beta-coefficients are quite similar to those we calculated in our multivariate regression models. In a study from Ohio (USA) serum vitamin D accounted for the largest amount of variance in serum total cholesterol (partial R =3.6%), triglycerides (partial R =3.1%), and LDL-C (partial R =2.9%) ($P < 0.0001$ for all) being also a significant positive explanatory variable for HDL-C (partial R = 1.4%, $P < 0.0001$) (6). In a meta-analysis with special reference to the effect of vitamin D on lipids all the cross-sectional studies showed that serum 25(OH)D was positively associated with HDL-C resulting in a favourable low-density lipoprotein cholesterol LDL-C (or total cholesterol) to HDL-C ratio (7). There is a uniform agreement of studies on a negative relation between serum 25(OH) D and triglycerides. On the other hand, the intervention studies gave divergent results (7). All these studies were based on general population samples. The situation is far more complex in the presence of type 2 diabetes. There are studies indicating a lack of impact of vitamin D on the clinical metabolic status (33), while others report controversial results (18,19).

Serum vitamin D and blood pressure

The relationship of blood pressure to serum vitamin D is also a matter of debate in the literature. In cross-sectional studies 25(OH)D is more closely associated to systolic (SBP) than to diastolic blood pressure (DBP) (8). Interventional studies with vitamin D supplementation reported either a decrease of only SBP (23), of both SBP and DBP (29), or no effect at

all (22,30). In the initial analysis we also registered a correlation of serum 25(OH)D with both SBP and DBP, although those with SBP were stronger. In the multivariate regression analysis however only SBP showed borderline relationship to the vitamin D status. A number of publications tried to dissect the nature of the association between vitamin D and high blood pressure (9,21). One of those meta-analyses showed that in phenotypic analyses high 25(OH) D concentrations were associated with decreased SBP (−0.12 mm Hg per 10% increase, p=0.003) and reduced odds of hypertension (odds ratio (OR) 0.98, p=0.0003), but not with decreased DBP (−0.02 mm Hg per 10% increase, p=0.37) (9). In another publication the associations of the genetic variants with the risk of vitamin D deficiency and BP showed a doubling of risk of vitamin D deficiency (21).

Serum vitamin D and glycemia

Even more complex is the association with plasma glucose in the fasting state and during the OGTT, as well as with plasma insulin levels and the calculated HOMA-IR. Data coming from the general population are controversial with some publications not able to find any association of serum vitamin D with glycemia, plasma insulin and insulin resistance (10), while others found an association with the HOMA-IR and plasma insulin levels (13,31) as well as with glucose tolerance (12). In an older study one month of vitamin D3 treatment decreased insulin resistance by 21.4%, but the change was not significant (26). Recent trials do not corroborate the hypothesis for a relationship between vitamin D status and glycemic control and insulin sensitivity in pre-diabetes and type 2 diabetes (24, 25), while others note some effect (32). We were able to find an association with plasma insulin and the HOMA-IR index in the whole study population, but there was no relationship with plasma glucose or insulin levels during the OGTT.

Additional findings

As a collateral finding we were also able to prove an inverse relationship with the levels of hsCRP, a marker of chronic inflammation. This correlation is also debatable as other studies reported lack of impact of low vitamin D status on biomarkers of cellular inflammation (33).

The inverse relationship of the percentage body fat to the serum vitamin D is not surprising as it is in line with the decreasing levels of vitamin D with increasing weight. As body composition analysis is more accurate in predicting obesity than simply measuring body weight, the correlation coefficients with vitamin D are higher for % body fat, than for weight in kilograms. Therefore, BIA might prove as a more sensitive tool for screening of subjects at risk for vitamin D deficiency.

All these evidence must be viewed with caution. The relationship of vitamin D (fat soluble vitamin) with metabolic parameters might be interpreted in both directions – obesity leading to low vitamin D levels or low vitamin D levels leading to obesity (20,34). However, building subgroups according to BMI led to loss of statistical significance most probably due to the small sample size. However BMI was included in the multivariate model as a basal variable. Other investigators have also noted this lack of direct relationship with BMI (35).

Our study was not designed to investigate the causal relationship between vitamin D and metabolic parameters. However it is worthy to mention that vitamin D is implicated in the regulation of energy balance (36). The active metabolite can regulate different cellular processes such as cell proliferation, differentiation and apoptosis (36).

The major advantage of our study is that it combined data coming from different investigation methods - BIA, anthropometry and assessment of metabolic health (lab data, including OGTT), thus allowing a complex description of the relations of vitamin D to obesity and the metabolic status. Its major disadvantage is the modest sample size, preventing our results from reaching statistical significance in specific subgroups based on age or BMI.

Our data corroborate the hypothesis for a weak association of the vitamin D status with several metabolic parameters such as lipids, fasting plasma glucose and blood pressure in some population samples. Whether this relationship is causal or low vitamin D is only a marker of low health status together with the metabolic parameters, cannot be answered by this study. Lipid levels and percentage body fat seem suited for predicting an increased risk of low vitamin D levels, thus adding information to simple measures of overweight and obesity.

In conclusion, although the association on the individual level might not always be present, vitamin D deficiency and insufficiency are very common in patients with poor metabolic health. Therefore, vitamin D supplementation should be regarded as a therapeutic option in all subjects with overweight, obesity and metabolic disturbances.

Conflict of interest

All authors declare no personal circumstances or interest that may be perceived as inappropriately influencing the representation or interpretation of reported research results.

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