

Article

Vitamin D Deficiency Is Associated with Impaired Sensitivity to Thyroid Hormones in Euthyroid Adults

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Table S1. The clinical characteristics in men and women.

Variables	Vitamin D sufficiency ($\geq 20\text{ng/mL}$)		Vitamin D deficiency ($< 20\text{ng/mL}$)		<i>p</i>
	Men	Women	Men	Women	
N	836	458	1176	673	NA
Age (years)	46.5 \pm 11.0	49.3 \pm 12.8 [†]	44.3 \pm 11.7 ^{&}	51.0 \pm 11.4 [#]	<0.001
BMI (kg/m ²)	25.74 \pm 3.11	23.38 \pm 3.55 [†]	25.82 \pm 3.46	23.84 \pm 3.64 [#]	<0.001
SBP (mmHg)	126.73 \pm 16.52	120.84 \pm 19.55 [†]	126.66 \pm 15.78	124.47 \pm 19.79 ^{#, \$}	<0.001
DBP (mmHg)	76.70 \pm 11.84	69.81 \pm 10.54 [†]	76.64 \pm 11.24	71.42 \pm 11.49 [#]	<0.001
ALT (U/L)*	24.0(18.0-34.0)	17.0(14.0-22.0) [†]	25.0(18.0-35.0)	17.0(14.0-23.0) [#]	<0.001
AST (U/L)*	23.0(20.0-27.0)	21.0(18.0-24.0) [†]	22.0(19.0-27.0)	21.0(18.0-24.0) [#]	<0.001
Urea (mmol/L)	5.54 \pm 1.26	5.07 \pm 1.20 [†]	5.43 \pm 1.20	5.03 \pm 1.34 [#]	<0.001
Cr (umol/L)	74.85 \pm 11.18	56.23 \pm 7.89 [†]	73.08 \pm 10.03 ^{&}	54.82 \pm 9.39 [#]	<0.001
UA (umol/L)	400.15 \pm 79.55	305.68 \pm 66.01 [†]	397.31 \pm 80.39	290.37 \pm 64.40 ^{#, \$}	<0.001
Ca (mmol/L)	2.40 \pm 0.09	2.39 \pm 0.09	2.40 \pm 0.09	2.37 \pm 0.08 ^{#, \$}	<0.001
P (mmol/L)	1.10 \pm 0.14	1.23 \pm 0.15 [†]	1.10 \pm 0.16	1.23 \pm 0.35 [#]	<0.001
25(OH)D (ng/mL)	26.20 \pm 5.93	26.15 \pm 6.15	14.84 \pm 3.19 ^{&}	13.90 \pm 3.56 ^{#, \$}	<0.001
TC (mmol/L)	5.00 \pm 0.92	5.14 \pm 0.98	5.02 \pm 0.92	5.24 \pm 1.12 [#]	<0.001
TG (mmol/L)*	1.44(1.03-2.04)	1.10(0.83-1.63) [†]	1.56(1.06-2.29) ^{&}	1.23(0.90-1.71) [#]	<0.001
HDL-C (mmol/L)	1.20 \pm 0.27	1.50 \pm 0.38 [†]	1.18 \pm 0.27	1.45 \pm 0.36 [#]	<0.001
LDL-C (mmol/L)	3.11 \pm 0.83	3.01 \pm 0.89	3.12 \pm 0.84	3.13 \pm 0.92	0.121
Non-HDL-C (mmol/L)	3.80 \pm 0.87	3.64 \pm 0.96 [†]	3.84 \pm 0.90	3.80 \pm 0.98 [#]	0.001
RC (mmol/L)*	0.61(0.39-0.88)	0.59(0.37-0.80)	0.61(0.39-0.88)	0.62(0.40-0.83)	0.334
AIP	0.107 \pm 0.279 ^{&}	-0.092 \pm 0.278 [†]	0.152 \pm 0.305	-0.043 \pm 0.287 ^{#, \$}	<0.001
Lp(a) (mmol/L)*	11.65(6.63-21.10)	14.80(8.28-29.15) [†]	11.10(6.50-22.40)	15.20(8.70-29.00)	<0.001
Glucose (mmol/L)*	4.98(4.59-5.45)	4.87(4.57-5.29) [†]	4.96(4.60-5.39)	4.92(4.58-5.34)	0.004
HbA1c (%)*	5.5(5.3-5.8)	5.6(5.3-5.9)	5.5(5.3-5.8)	5.6(5.3-5.8)	0.836
Insulin (mIU/L)*	7.9(5.7-11.3)	7.4(5.3-10.8)	8.7(5.9-12.2) ^{&}	7.9(5.5-10.8) [#]	<0.001
HOMA-IR*	1.80(1.25-2.72)	1.67(1.11-2.40)	1.95(1.28-2.96)	1.72(1.17-2.50) [#]	<0.001
HOMA- β *	109.40(70.82-166.67)	109.23(75.51-160.65)	117.75(75.00-184.88)	111.26(76.64-164.91)	0.057
HOMA-ISI*	0.025(0.016-0.036)	0.027(0.019-0.040)	0.023(0.016-0.035)	0.026(0.018-0.038) [#]	<0.001

TyG (mg/dL) ²	8.73±0.60	8.45±0.55 [†]	8.81±0.67 ^{&}	8.55±0.58 [#]	<0.001
FT3 (pg/mL)	3.37±0.31	3.05±0.28 [†]	3.41±0.32	3.10±0.32 [#]	<0.001
FT4 (ng/dL)	1.30±0.15	1.23±0.14 [†]	1.32±0.16	1.25±0.14 ^{#, \$}	<0.001
TSH (uIU/mL)	1.90±0.84	2.18±0.98 [†]	1.93±0.82	2.51±1.02 ^{#, \$}	<0.001
Anti-TG positivity, n (%)	43(5.1%)	66(14.4%) [†]	71(6.0%)	114(16.9%)*	<0.001
Anti-TPO positivity, n (%)	45(5.4%)	66(14.4%) [†]	74(6.3%)	99(14.7%)*	<0.001
TFQI	-0.032±0.382	-0.090±0.395 [†]	0.014±0.386 ^{&}	0.068±0.352 ^{#, \$}	<0.001
PTFQI	0.023±0.386	-0.036±0.398 [†]	0.068±0.389 ^{&}	0.123±0.355 ^{#, \$}	<0.001
TSHI	2.80±0.48	2.80±0.51	2.85±0.49	3.00±0.47 ^{#, \$}	<0.001
TT4RI	31.64±14.26	34.30±15.62 [†]	32.57±14.02	40.09±16.07 ^{#, \$}	<0.001
FT3/FT4	0.314±0.038	0.301±0.039 [†]	0.313±0.041	0.299±0.039 [#]	<0.001

*Non-normally distributed continuous variables were compared after natural log transformation. Continuous variables were analyzed by one-way ANOVA with tukey's post hoc test. Categorical variables were compared with Fischer's exact tests. [†]: significant difference between men and women in the vitamin D sufficiency group; [#]: significant difference between men and women in the vitamin D deficiency group; [&]: significant difference between the vitamin D sufficiency group and the vitamin D deficiency group in men; ^{\$}: significant difference between the vitamin D sufficiency group and the vitamin D deficiency group in women. Abbreviations: NA, not applicable; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; UA, uric acid; 25(OH)D, 25-hydroxyvitamin D; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; AIP, atherogenic index of plasma; Lp(a), lipoprotein a; Ca, calcium; P, phosphorus; HbA1c, Hemoglobin A1c; HOMA-IR, homeostatic model for insulin resistance; HOMA-β, homeostatic model β; HOMA-ISI, homeostatic model for insulin sensitivity index; TyG, triglyceride-glucose index; FT3, free thyroxine; FT4, free thyrotropin; TSH, thyroid-stimulating hormone; Anti-TG, antithyroglobulin; Anti-TPO, antithyroidperoxidase. TFQI, thyroid feedback quartile-based index; PTFQI, parametric thyroid feedback quartile-based index; TSHI, TSH index; and TT4RI, thyrotropin thyroxine resistance index.

Table S2. The relationship between 25(OH)D levels and thyroid-associated variables after adjusting for age, BMI, DBP, TG, glucose, ALT, Cr, and UA in men and women.

Variables	Men		Women	
	r	p	r	p
FT3 (pg/mL)	-0.001	0.977	-0.068	0.023
FT4 (ng/dL)	-0.001	0.958	-0.101	0.001
TSH (uIU/mL)	-0.038	0.088	-0.144	<0.001
TFQI	-0.027	0.220	-0.198	<0.001
PTFQI	-0.028	0.214	-0.198	<0.001
TSHI	-0.040	0.073	-0.183	<0.001
TT4RI	-0.039	0.082	-0.167	<0.001
FT3/FT4	-0.002	0.920	0.041	0.167

Data was analyzed by Pearson's and partial correlation coefficients. Abbreviations: 25(OH)D, 25-hydroxyvitamin D; FT3, free triiodothyronine; FT4, free thyrotropin; TSH, thyroid-stimulating hormone; TFQI, thyroid feedback quartile-based index; PTFQI, parametric thyroid feedback quartile-based index; TSHI, TSH index; TT4RI, thyrotropin thyroxine resistance index; BMI, body mass index; DBP, diastolic blood pressure; TG, triglyceride; ALT, alanine aminotransferase; Cr, creatinine; and UA, uric acid.

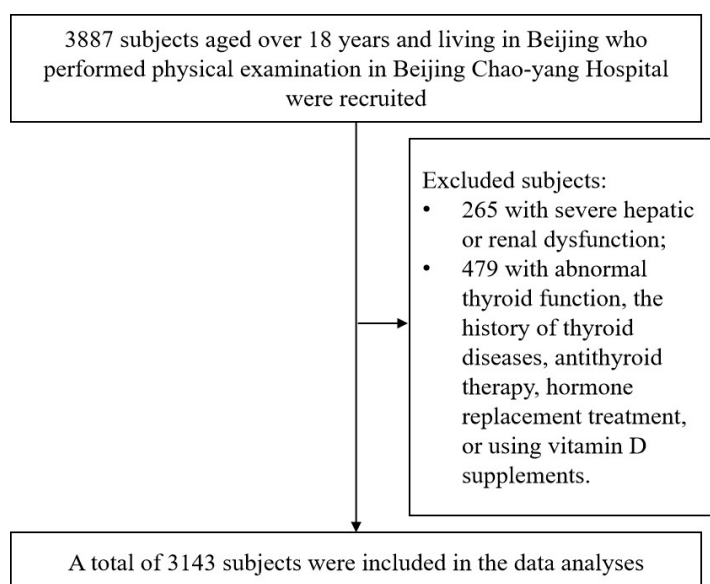


Figure S1. Flowchart of this study.

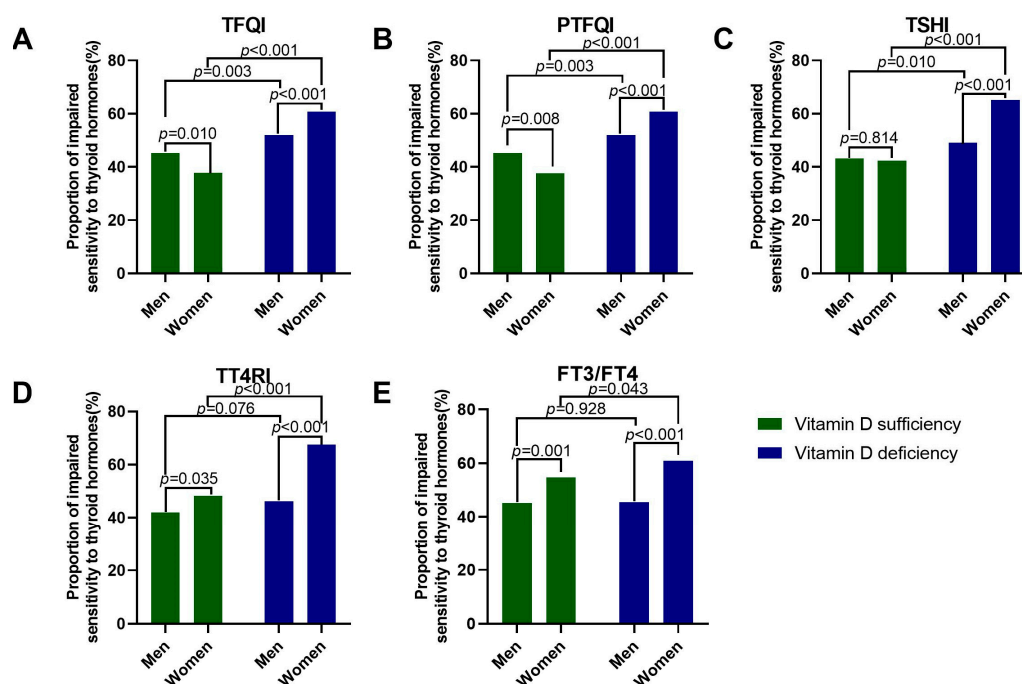


Figure S2. The proportions of participants with impaired sensitivity to thyroid hormones in men and women in the vitamin D sufficiency group and the vitamin D deficiency group. Data was analyzed by Fisher's exact test. (A) TFQI; (B) PTFQI; (C) TSHI; (D) TT4RI; and (E) FT3/FT4. TFQI, thyroid feedback quartile-based index; PTFQI, parametric thyroid feedback quartile-based index; TSH, thyroid-stimulating hormone; TSHI, TSH index; TT4RI, thyrotropin thyroxine resistance index; FT3, free triiodothyronine; and FT4, free thyrotropin.