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High Prevalence of Severe Vitamin D Deficiency in cART Naïve and Successfully Treated Swiss HIV Patients

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SWISS HIV COHORT STUDY

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BACKGROUND

Recent studies have increased the awareness of beneficial effects of vitamin D. Besides being essential for bone growth and preservation, antineoplastic and immunmodulatory effects have been described.

Considering the high prevalence of osteopenia (up to 60%) and osteoporosis (up to 15%) as well as the increasing number of neoplasias, adequate vitamin D levels seem particularly important in the HIV-population.

AIMS

To determine vitamin D levels in HIV-positive patients comparing measurements by season as well as before and after the initiation of cART. To look for predictors for vitamin D deficiency.

PATIENTS AND METHODS

25(OH) vitamin D was measured in 211 HIV-positive patients (**Table1**).

Samples were taken **before initiation of cART** from Feb-Apr (**nadir sun exposure**) or from Aug-Oct (**maximal sun exposure**) as well as 12 (same season) and 18 months (alternate season) **after starting cART**.

We defined values <30 nmol/L as vitamin D deficiency, while 75 nmol/L 25(OH)D was set as minimal target .

$1,25(OH)_2$ vitamin D was measured in a subset of 74 patients.

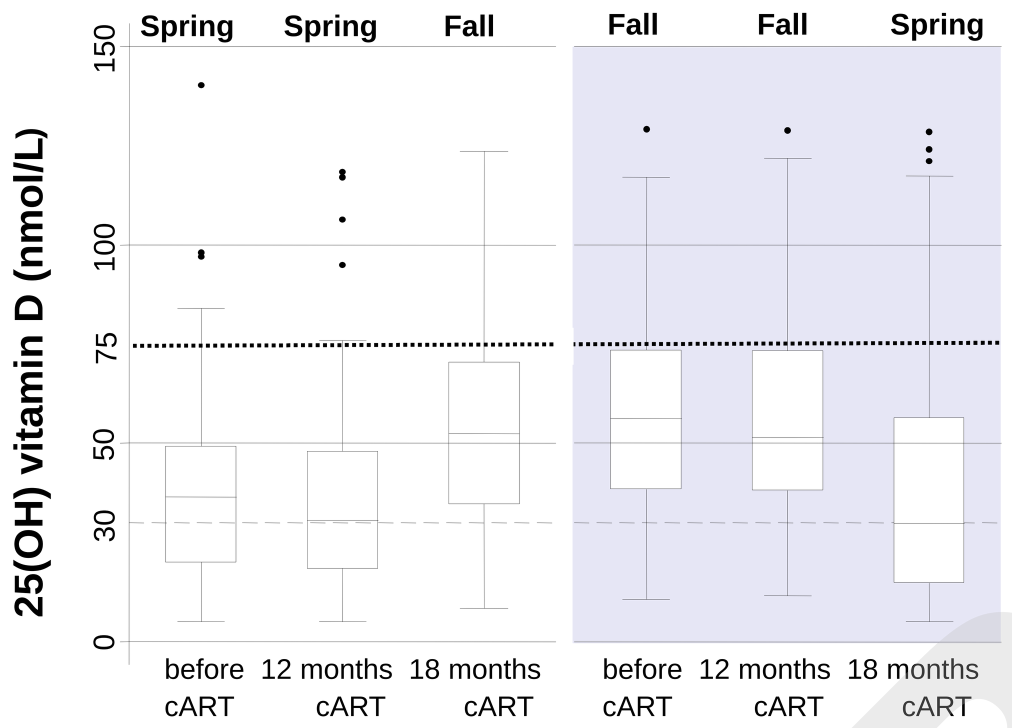
Table 1:		
Baseline characteristics	**Fall (n = 108)**	**Spring (n = 103)**
Male gender	80 (74%)	78 (76%)
Age in years	38 (33-44)	36 (31-45)
Caucasian	93 (86%)	92 (89%)
Previous AIDS	15 (14%)	15 (15%)
HIV transmission		
homosexual	35 (32%)	50 (48%)
heterosexual	54 (50%)	42 (41%)
iv drug use	19 (18%)	11 (11%)
CD4 cells/mL	223 (136-317)	230 (135-352)
BMI (kg/m2)	22.6 (20.4-25.4)	23.1 (21.2-25.2)
cGFR (mL/min)	105 (91-124)	109 (98-120)
future cART		
+TDF	20 (19%)	15 (15%)
+NNRTI	53 (49%)	38 (37%)
+PI	55 (51%)	63 (61%)
neither NNRTI nor PI	7 (6%)	8 (8%)

RESULTS

25(OH) vitamin D

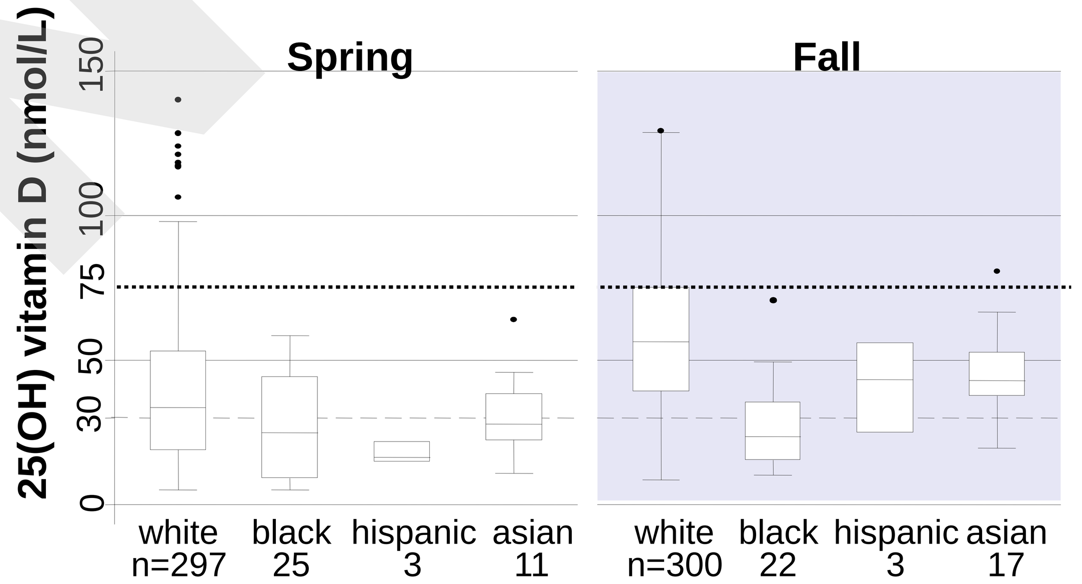
At each timepoint, 25(OH)D levels were significantly higher in fall than in spring (p <0.001), without significant change with respect to cART.

With 42%-52%, vitamin D deficiency was three times more frequent during springtime than in fall.



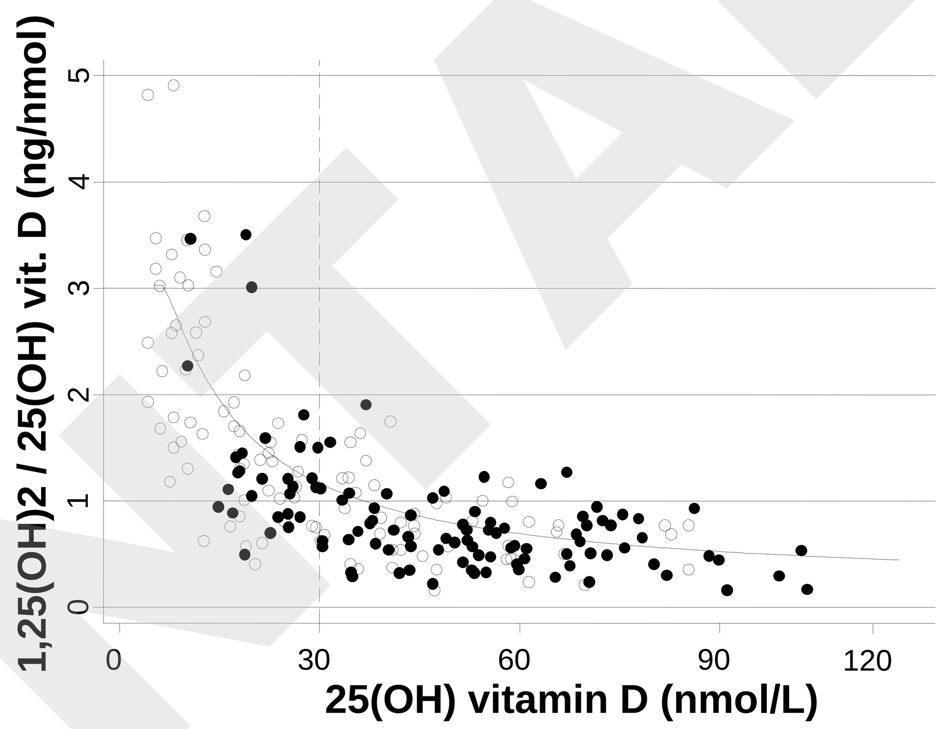
Baseline before cART:	**Fall (n=108)**	**Spring (n=103)**
Vitamin D deficiency	14%	42%
insufficiency	62%	53%
target level	24%	5%
12 months after cART start:	**Fall**	**Spring**
Vitamin D deficiency	14%	47%
insufficiency	63%	48%
target level	23%	5%
18 months after cART start:	**Fall**	**Spring**
Vitamin D deficiency	18%	52%
insufficiency	59%	38%
target level	23%	10%

Ethnicity was a significant predictor for serum 25(OH)D values (p<0.001). In both seasons, Caucasians had a lower prevalence of vitamin D deficiency and insufficiency



$1,25(OH)_2$ vitamin D

Correlating the 1,25(OH)2D to 25(OH)D ratio with 25(OH)D levels (below) indicates an exponential increase of 1-hydroxylation (i.e. vitamin D activation) with decreasing 25(OH)D levels. Black circles indicate measurements in fall, white circles in spring. This compensatory increase in renal 1-alpha-hydroxylation with decreasing 25(OH)D levels resulted in a less pronounced seasonal swing for 1,25(OH)2D (minus 3-13%) than for 25(OH)D (minus 36-43%).



	Baseline before cART		**12 months after cART initiation**		**18 months after cART initiation**	
	25(OH)D	**$1,25(OH)_2D$**	**25(OH)D**	**$1,25(OH)_2D$**	**25(OH)D**	**$1,25(OH)_2D$**
Fall	57 (39-74)	39 (26-58)	51 (38-73)	36 (27-46)	53 (35-70)	34 (25-49)
Spring	37 (20-49)	34 (24-48)	31 (19-48)	32 (23-44)	30 (15-57)	33 (22-47)
Difference	**-36%**	-13%	**-40%**	-11%	**-43%**	-3%
p-value	**<0.001**	0.07	**<0.001**	0.3	**<0.001**	0.4

Uni- and multivariable regression analyses of parameters influencing serum 25(OH) and $1,25(OH)_2$ vitamin D levels

	25(OH)D				**$1,25(OH)_2D$**			
	Univariable Coeff (95% CI)	p-value	Multivariable Coeff (95% CI)	p-value	Univariable Coeff (95% CI)	p-value	MultivariableCoeff (95% CI)[1]	p-value
Female sex	-3.5 (-8.4; 1.4)	0.2	-4.2 (-10.2; 1.9)	0.2	4.9 (-11.0; 1.3)	0.1	1.4 (-6.3; 9.1)	0.7
Age by 10 yrs	0.8 (-1.2; 2.9)	0.4	0.1 (-2.6; 2.8)	1.0	1.1 (-1.1; 3.4)	0.3	-2.3 (-5.3; 0.8)	0.1
Caucasian	**17.1 (10.7; 23.6)**	**<0.001**	**14.1 (6.0; 22.1)**	**0.001**	-2.1 (-13.3; 9.1)	0.7	-3.6 (-16.0 ; 8.8)	0.6
BMI	-0.4 (-1.0; 0.2)	0.2	-0.7 (-1.5; 0.0)	0.05	**0.7 (0.0; 1.5)**	0.04	**1.7 (0.8; 2.6)**	<0.001
Active IDU	-5.0 (-13.2; 3.2)	0.2	**-11.2 (-21.0; -1.5)**	**0.02**	-5.8 (-21.3; 9.8)	0.5	-14.1 (-31.6; 3.5)	0.1
HCV positivity	-7.1 (-15.5; 1.2)	0.1	-7.8 (-17.5; 1.9)	0.1	-4.4 (-12.0; 3.2)	0.3	**-9.1 (-17.8; -0.4)**	0.04
cGFR <60 mL/min	21.3 (-1.4; 44.0)	0.07	8.6 (-17.6; 34.8)	0.5	1.3 (-17.7; 20.3)	0.9	2.8 (-22.0: 27.7)	0.8
Duration of HIV by 10 yrs	**6.9 (2.9; 11.0)**	**0.001**	**6.4 (1.2; 11.7)**	**0.02**	1.5 (-2.8; 5.8)	0.5	5.5 (-0.2; 11.0)	0.06
Previous AIDS	2.1 (-3.6; 7.8)	0.5	1.4 (-4.9; 7.7)	0.7	-4.9 (-11.9; 2.1)	0.2	**-11.6 (-20.0; -3.2)**	**0.007**
CD4 count by 100 cells/uL	-0.2 (-1.2; 0.7)	0.6	0.2 (-0.9; 1.3)	0.7	**-1.6 (-2.9; -0.3)**	0.02	**-2.6 (-4.3; -0.9)**	0.003
Spring vs. Fall	**-19.2 (-23.2; -15.2)**	**<0.001**	**-17.7 (-22.5; -13.0)**	**<0.001**	**-5.7 (-10.7; -0.7)**	0.03	-4.4 (-9.8; 1.1)	0.1
TDF use	4.1 (-3.4; 11.6)	0.3	3.8 (-3.8; 11.4)	0.3	**10.4 (4.5; 16.2)**	0.001	**7.8 (1.1; 14.6)**	0.02
NNRTI use	**-8.7 (-14.0; -3.5)**	**0.001**	**-8.2 (-13.3; -3.0)**	**0.002**	**6.2 (0.1; 12.2)**	0.05	1.8 (-4.2; 7.8)	0.5

CONCLUSIONS

- **With 42-52% in spring and 14-18% in fall, vitamin D deficiency was highly prevalent**
- **Black ethnicity was a significant risk factor for vitamin D deficiency**
- **NNRTI-use was associated with significantly lower 25(OH)D levels**
- **TDF-use correlated with higher serum $1,25(OH)_2D$ and serum alkaline phosphatase levels**
- **we suggest systematic screening for vitamin D deficiency in all HIV-positive patients**