Vitamin D Status and Hepatic Steatosis in People with HIV: Evidence from Paired Measurements

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Background

Vitamin D insufficiency and hepatic steatosis are highly prevalent in people with HIV (PWH).

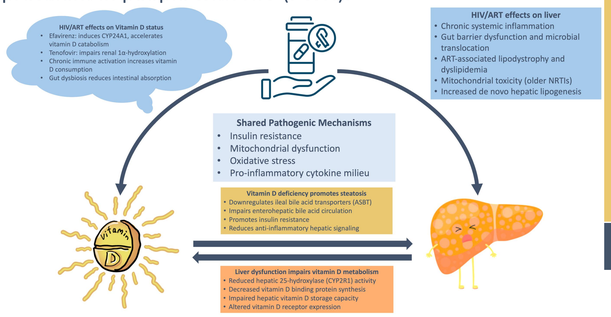


Figure 1. *The relationship between (i) HIV and antiretroviral therapy, (ii) vitamin D defficiency and (iii) hepatic steatosis.*

Vitamin D plays pleiotropic roles in immune regulation, insulin sensitivity, lipid metabolism, and fibrogenesis. Experimental and clinical data suggest that low serum vitamin D may contribute to hepatic fat accumulation and fibrosis progression. Conversely, hepatic steatosis may impair vitamin D metabolism, creating a potentially bidirectional relationship (Figure 1).

The objective of the study was to assess the relationship between serum vitamin D levels and hepatic steatosis severity in a prospective cohort with paired transient elastography (TE) and vitamin D measurements.

Methods

- This was a longitudinal observational cohort study including PWH from Modena HIV Metabolic Clinic.
- PWH with at least two visits in which transient elastography (TE) and serum vitamin D were measured concurrently were eligible for inclusion.
- Hepatic steatosis severity was assessed using the controlled attenuation parameter (CAP), expressed in dB/m (Figure 2).

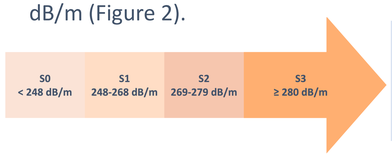


Figure 2. *CAP cut-offs to define severity of hepatic steatosis.*

- Routinely, all PWH were offered vitamin D supplementation at a weekly dose of 10,000 IU/mL, according to standard clinical practice. Adherence to supplementation was not systematically measured.
- Multivariable mixed-effects linear regression was applied with CAP as the dependent variable, adjusting for age, sex, BMI, waist circumference, diabetes, CD4 count, HIV suppression, and ART class.

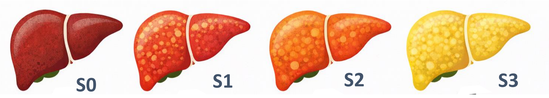
Lower vitamin D levels were consistently linked to more severe hepatic steatosis among people with HIV. This relationship persisted even after accounting for differences in body weight, metabolic parameters, and HIV-related factors, suggesting vitamin D status may play a meaningful role in liver health.

Results

- A total of 6579 observations from 1614 PWH were analyzed (median age 56 years; 72% male). Baseline characteristics are shown in Table 1. Median follow-up time was 4.10 (Q1, Q3: 1.23, 5.56) years.

Table 1. *Baseline characteristics of the population according to liver steatosis severity.*

Median (Q1, Q3) or N (%)	S0 N = 974 (60.3%)	S1 N = 199 (12.3%)	S2 N = 93 (5.8%)	S3 N = 348 (21.6%)	p
Age, years	56 (50, 61)	56 (53, 61)	58 (54, 64)	58 (53, 63)	**<0.001**
Male sex	679 (70%)	149 (75%)	70 (75%)	276 (79%)	**0.005**
BMI, kg/m²	23.0 (21.0, 25.3)	24.9 (23.0, 27.0)	26.4 (24.9, 28.7)	27.1 (24.8, 30.6)	**<0.001**
Waist circumference, cm	86 (80, 93)	93 (86, 100)	98 (91, 105)	101 (94, 110)	**<0.001**
Sedentary lifestyle	378 (39%)	82 (41%)	38 (41%)	195 (56%)	**<0.001**
Total cholesterol, mg/dl	181 (153, 205)	183 (145, 218)	174 (137, 214)	174 (143, 204)	0.200
LDL cholesterol, mg/dl	113 (90, 136)	118 (87, 141)	107 (77, 142)	110 (85, 136)	0.300
HDL cholesterol, mg/dl	53 (44, 63)	48 (42, 59)	50 (42, 57)	46 (39, 54)	**<0.001**
Tryglicerides, mg/dl	95 (71, 130)	122 (87, 163)	116 (83, 158)	126 (89, 199)	**<0.001**
HOMA-IR	1.55 (0.98, 2.29)	2.27 (1.53, 3.01)	3.01 (1.91, 4.19)	3.15 (1.81, 5.53)	**<0.001**
HbA1C, mmol/mol	34 (30, 37)	35 (32, 38)	35 (31, 38)	37 (33, 42)	**<0.001**
Time since HIV diagnosis, years	25 (16, 32)	26 (18, 31)	25 (18, 31)	26 (19, 32)	0.300
Current CD4 cell count, c/microL	690 (527, 901)	742 (590, 955)	688 (540, 871)	732 (585, 956)	**<0.001**
CD4/CD8 ratio	0.94 (0.68, 1.36)	1.00 (0.66, 1.40)	0.89 (0.69, 1.23)	0.89 (0.65, 1.22)	0.200
Current exposure to NNRTI	328 (34%)	61 (31%)	33 (35%)	125 (36%)	0.600
Current exposure to PI	195 (20%)	44 (22%)	10 (11%)	57 (16%)	0.055
Current exposure to INSTI	674 (69%)	147 (74%)	63 (68%)	240 (69%)	0.600
Diabetes	32 (3.3%)	7 (3.5%)	6 (6.5%)	30 (8.6%)	**<0.001**
Hypertension	184 (19%)	49 (25%)	20 (22%)	107 (31%)	**<0.001**
SCORE-2	4.9 (3.4, 7.3)	5.8 (3.8, 8.5)	6.2 (4.5, 8.4)	6.8 (4.8, 9.4)	**<0.001**
Liver stiffness, kPa	4.80 (4.00, 6.00)	5.40 (4.40, 6.70)	5.30 (4.30, 6.70)	6.30 (5.20, 8.10)	**<0.001**
CAP, dB/m	211 (190, 229)	257 (252, 263)	274 (271, 277)	310 (294, 332)	**<0.001**



Vitamin D levels (ng/ml)			
33 (26, 41)	33 (25, 39)	30 (23, 39)	28 (21, 35)

Figure 3. *Vitamin D levels and steatosis severity.*

Table 2. *Multivariable mixed-effects regression for CAP (dB/m).*

Variable	β coefficient	95% CI	p
25(OH)D (per 1 ng/mL)	−0.31	−0.43 to −0.18	**<0.001**
Age (per year)	−0.22	−0.46 to +0.03	0.081
Male sex (vs female)	−1.23	−5.97 to +3.51	0.611
BMI (per kg/m²)	+2.17	+1.58 to +2.75	**<0.001**
Waist circumference (cm)	+1.59	+1.37 to +1.81	**<0.001**
Diabetes (yes vs no)	−6.61	−13.33 to +0.11	0.054
HIV RNA undetectable	+0.29	−8.18 to +8.77	0.946
CD4 count (per cell/μL)	−0.0016	−0.0023 to −0.0008	**<0.001**
PI use (yes vs no)	−0.97	−5.71 to +3.78	0.690
NNRTI use (yes vs no)	−1.82	−6.13 to +2.49	0.409
INSTI use (yes vs no)	−3.48	−7.94 to +0.97	0.126

Discussion and Conclusions

- In this large cohort of PWH, lower serum 25(OH)D levels were independently associated with greater hepatic steatosis severity. The association persisted after adjustment for adiposity, metabolic burden, and HIV-related factors, and remained consistent in longitudinal mixed-effects analyses.
- Biological plausibility supports a potential interaction between vitamin D status and hepatic steatosis, through mechanisms involving insulin resistance, inflammation, and altered lipid metabolism. In the context of HIV, chronic immune activation and ART-related metabolic changes may further amplify this relationship.
- However, this is an observational study and does not establish causality. Residual confounding cannot be excluded, and unmeasured factors such as diet, sunlight exposure, physical activity, seasonal variability, genetic determinants, and adherence to supplementation may have influenced the findings.
- These findings highlight vitamin D status as a potential component of the metabolic–hepatic axis in HIV care.
- Prospective and interventional studies are needed to determine whether correction of vitamin D deficiency can modify hepatic steatosis progression in this population.

PLAIN LANGUAGE SUMMARY

In people with HIV, lower vitamin D levels were linked to more severe fat accumulation in the liver. Although this study does not prove cause and effect, it suggests that vitamin D may play a role in liver health in this population.

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