



Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS

# Zinc deficiency and advanced liver fibrosis among HIV/HCV co-infected persons in Russia

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## BACKGROUND

### Introduction

- Russia is currently experiencing converging epidemics of HIV, hepatitis C virus (HCV), and alcohol use disorder.
- HIV accelerates liver fibrosis in the setting of HCV co-infection and alcohol use.
- Zinc deficiency is common among people living with HIV and is also common in Russia.
- Zinc deficiency may be one of the factors that facilitates the underlying mechanisms of liver fibrosis.

### Aim

- We investigated the association between zinc deficiency and advanced liver fibrosis in a cohort of HIV/HCV co-infected persons reporting heavy drinking in Russia.

## METHODS

### Study Design:

- Secondary data analysis of baseline data from ZINC RCT (N=204), a double-blinded randomized placebo-controlled trial, of zinc supplementation

### Inclusion Criteria:

- 1) HIV+; 2) HCV+; 3) 18-70 years; 4) past month heavy alcohol use (i.e., NIAAA risky drinking amounts); 5) documented ART-naïve at enrollment; 6) 2 contacts; 7) live within 100 km of St. Petersburg; 8) phone

### Exclusion Criteria

- 1) not fluent in Russian; 2) cognitively impaired; 3) breastfeeding or pregnant

### Main Independent Variable:

- Zinc deficiency was defined as plasma zinc <0.75 mg/L at baseline.

### Outcome:

- Advanced liver fibrosis, defined as either (1) FIB-4 >3.25, (2) FIB-4 ≥1.45 and ≤3.25 with elastography suggestive of advanced liver fibrosis (≥10.5 kpa), or (3) APRI ≥1.5.

### Statistical Analyses:

- Multivariable regression models adjusted for potential confounders: demographics, BMI, HIV-related factors, and substance use.

## RESULTS

**Table 1. Patient demographic and clinical characteristics of HIV and HCV co-infected ART naïve Russians**

	Overall (n=204)	Zinc deficiency (n=65)	Normal zinc levels (n=136)	p value
Age, mean (SD)	33.6 (5.2)	33.9 (5.5)	33.5 (5.0)	0.58
Gender, male, (%)	154 (75.5%)	48 (73.8%)	106 (76.3%)	0.71
Time since HIV diagnosis, years, mean (SD)	7.5 (4.8)	8.1 (4.6)	7.2 (4.9)	0.23
CD4 count, median (25 <sup>th</sup> , 75 <sup>th</sup> percentile)	463.7 (294.2, 700.1)	423.4 (256.8, 709.7)	471.2 (304.0, 697.5)	0.60
CD4 count (%)				0.31
<350	68 (33.3%)	25 (38.5%)	43 (30.9%)	
350-500	48 (23.5%)	17 (26.2%)	31 (22.3%)	
>500	88 (43.1%)	23 (35.4%)	65 (46.8%)	
HIV viral load (Log <sub>10</sub> IU/mL), median (25 <sup>th</sup> , 75 <sup>th</sup> percentile)	4.4 (3.6, 5.1)	4.4 (3.7, 4.6)	4.4 (3.4, 5.2)	0.52
Hepatitis B antibody positive, yes (%)	72 (35.3%)	21 (32.3%)	51 (36.7%)	0.54
Body Mass Index, mean (SD)	22.9 (3.1)	22.8 (3.1)	22.9 (3.1)	0.92
Alcohol abuse/dependence, yes (%)	179 (88.2%)	58 (89.2%)	121 (87.7%)	0.82
Alcohol consumption past 30 days				0.56
Heavy drinking	190 (93.1%)	62 (95.4%)	128 (92.1%)	
Moderate drinking	14 (6.9%)	3 (4.6%)	11 (7.9%)	
Current cocaine use, yes (%)	4 (2.0%)	1 (1.6%)	3 (2.2%)	1
Past 30-day injection drug use, yes (%)	84 (41.8%)	26 (41.3%)	58 (42.0%)	1
Advanced fibrosis, yes (%)	50 (24.5%)	18 (27.7%)	32 (23.0%)	0.47

**Table 2. Association between zinc deficiency and advanced liver fibrosis, logistic regression models**

	Partially adjusted model		Fully adjusted model	
	Adjusted odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)	p value
<b>Zinc deficiency</b>	<b>1.25 (0.62-2.53)</b>	<b>0.54</b>	<b>1.28 (0.62-2.61)</b>	<b>0.51</b>
Time (years) since HIV diagnosis	1.02 (0.95-1.10)	0.57	1.02 (0.95-1.10)	0.61
Alcohol abuse or dependence	1.08 (0.37-3.22)	0.89	1.19 (0.37-3.85)	0.77
HIV viral load (Log <sub>10</sub> IU/mL)	1.15 (0.84-1.60)	0.39	1.14 (0.83-1.56)	0.41
CD4 count				
<350	2.31 (1.11-4.80)	0.02	2.20 (1.05-4.62)	0.04
350-500	0.46 (0.16-1.33)	0.15	0.44 (0.15-1.30)	0.14
>500 (Reference Group)	1	--	1.00	--
Age	--	--	0.98 (0.92-1.05)	0.61
Gender	--	--	0.70 (0.31-1.61)	0.40
Hepatitis B	--	--	1.42 (0.70-2.91)	0.33
BMI	--	--	0.99 (0.88-1.10)	0.83

## CONCLUSIONS

- In this cohort of Russians with HIV/HCV co-infection, who are anti-retroviral treatment naïve and have heavy alcohol use, we observed associations between zinc deficiency and onset of advanced liver fibrosis that were in the hypothesized direction but not statistically significant.

## Limitations

- Duration of zinc deficiency is unknown.
- Competing risks for fibrosis such as untreated HIV, HCV, HBV, alcohol use and injection drug use may limit our ability to detect a significant impact from zinc deficiency in this exploratory analysis.
- Post-hoc power calculations indicate the study was underpowered.

## Implications

- Future studies with larger sample sizes that examine the longitudinal association between chronic zinc deficiency and the rate of liver fibrosis progression among HCV-mono-infected and HIV/HCV co-infected persons would be of interest.

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