0254

Iron Metabolism In Chronic HIV: Impaired Hepcidin-Soluble Transferrin Receptor Axis

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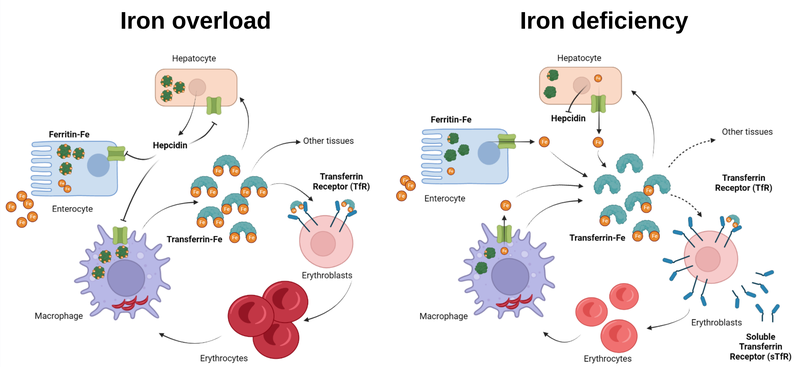
BACKGROUND

Chronic HIV-infected subjects under effective antiretroviral treatment (ART) exhibit an immune dysfunction leading to comorbidities. Since **iron metabolism plays an essential role in immune cell function**, its regulation may be relevant in this context.

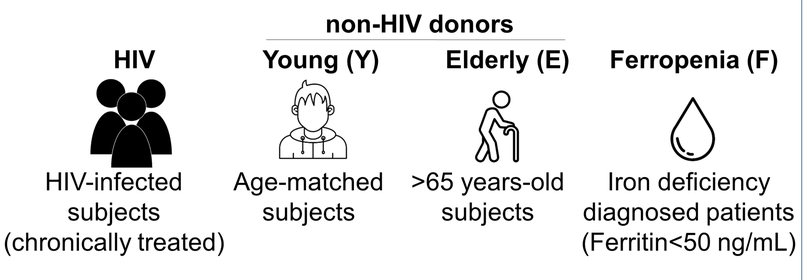
Iron is transported in plasma bound to transferrin, while is intracellularly stored by ferritin. The pool of transferrin supplies iron to all cells by binding to transferrin receptors (TfR). Also, a soluble truncated form of TfR (**sTfR**) is released to plasma during iron deficiency and reflects total TfR concentration. The main regulator of iron absorption is the hormone **hepcidin** which is released by the liver during iron overload.

Iron metabolism has been mainly studied in patients from low-income countries with malnutrition, opportunistic infections and limited access to treatment. These studies have not been carried out so far in **non-anemic asymptomatic chronic HIV infected patients**.



METHODS

Study groups: chronic HIV (n=92) and non-HIV donors (young and elderly groups; n=25 each). A ferropenic group (ferritin <50 ng/mL) (n=84) was only included as a reference group. Traditional biomarkers of iron metabolism, as well as soluble transferrin receptor (sTfR), hepcidin, and inflammatory markers were determined in plasma.



RESULTS

1. Characteristics of the study groups

Parameter	Young (N=25)	HIV (N=92)	Elderly (N=25)	*p* (K-W)*	*p* (M-W; Y vs. HIV)	*p* (M-W; Y vs. E)	*p* (M-W; HIV vs E)
Age (years)	40[30 - 58]	42[34 – 47]	82[78 - 88]	**<0.0001**	0.824	**<0.0001**	**<0.0001**
Males, n (%)	15(60)	87(95)	25(100)	**<0.0001**			
CD4 (cells/mm^3)	908[789 – 1031]	660[477 – 894]	625[509 - 755]	**0.003**	**0.001**	**0.003**	0.972
CD8 (cells/mm^3)	556[340 – 727]	719[602 – 1018]	341[182 - 436]	**<0.0001**	**<0.0001**	**0.004**	**<0.0001**
CD4/CD8 ratio	1.71[1.34 – 2.35]	0.75[0.56 – 1.33]	2.15[1.50 – 3.09]	**<0.0001**	**<0.0001**	0.207	**<0.0001**
CD4 nadir (cells/mm^3)	n/a	287[177-392]	n/a				
ART exposure (months)	n/a	37[26-39]	n/a				

Notes: Quantitative variables are expressed as median [IQR], and the categorical variable "Males" is expressed as the number of cases (%). Variables with a *p*-value <0.05 were considered statistically significant, as shown in bold. Abbreviations: K-W, nonparametric Kruskal-Wallis test; M-W, nonparametric Mann-Whitney *U* test; Y, Young; E, Elderly; ART, antiretroviral treatment; n/a, non-applicable.*For the qualitative variable "sex", a chi-square test was applied.

2. HIV-infected subjects exhibited altered levels of iron-related biomarkers but normal hepcidin levels

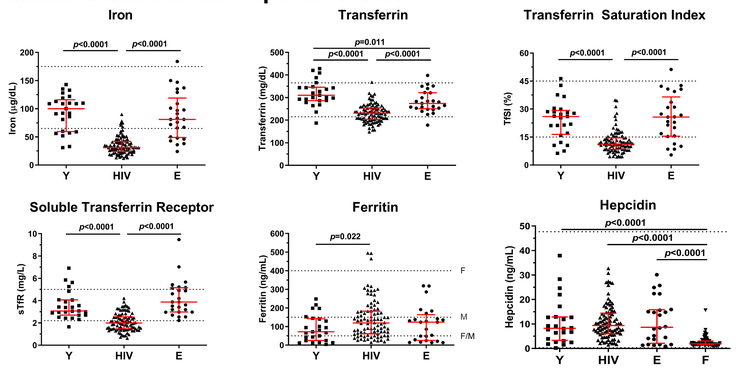


Figure 1. Levels of iron metabolism-related parameters in Y, HIV, and E groups. Hepcidin levels were also measured in F group. Grid lines represent minimum and maximum standard values; F, in females and M, in males.

3. HIV-infected subjects showed altered associations between sTfR or hepcidin and traditional iron-related parameters, which was even more evident in immunological non-recovered patients.

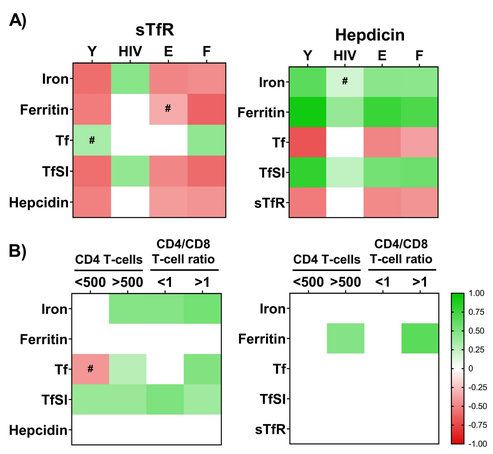


Figure 2. Interrelations between sTfR or hepcidin and iron metabolism parameters in: A) Y, HIV, E and F groups or B) immunological recovered vs. non-recovered HIV patients. Color intensity of boxes represents Spearman's rank correlation coefficient value as indicated in the color legend. All colored boxes represent statistically significant correlations, excepting for those noted as # ($0.05 \leq p \leq 0.1$).

Successfully-treated chronic HIV infection affects the homeostasis of iron metabolism modulators (sTfR and hepcidin).

4. HIV inflammatory profile differed from the Elderly, showing high levels of homocysteine and β2-microglobulin

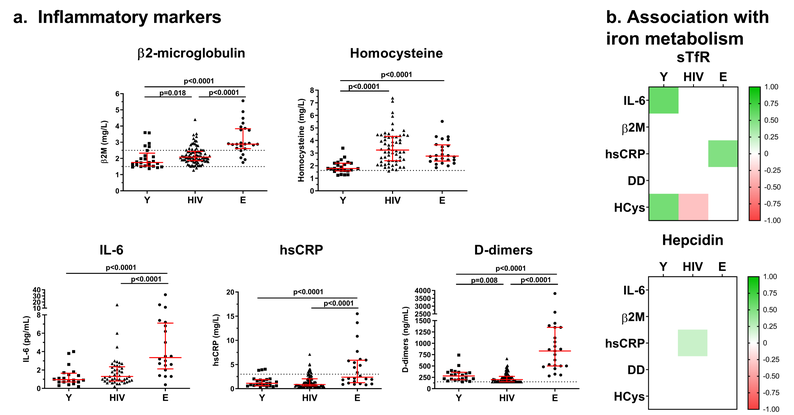


Figure 3. Inflammatory markers. a) Levels of markers quantified in Y, HIV, and E groups. Grid lines represent minimum and maximum standard values. b) Associations between sTfR or hepcidin and inflammatory markers. Color intensity boxes represents Spearman's rank coefficient value as indicated in the color legend.

CONCLUSION

Chronic HIV-infected patients under ART exhibit an imbalanced regulation of iron metabolism-related components, including hepcidin and sTfR, that is aggravated in immunological non-recovered patients, suggesting a complex functional iron deficiency that could contribute to their persisting immune dysfunction.

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