Abstract

Anaemiais a frequent comorbidity in HIV infection, driven in part by disruptions in iron regulation. While the role of hepcidin is well documented, the contributions of erythroferrone and hephaestin remain underexplored, especially in African cohorts. Thisstudyinvestigated the differential expression of these biomarkers across defined sub-categories of antiretroviral therapy (ART) exposure and adherence in Western Kenya with an aim to elucidate their contributions to iron deficiency anaemia(IDA) in HIV-infected individuals. A cross-sectional study was conducted at Busia County Referral Hospital among 163 adults comprising HIV infected ART-adherent (n = 47), ART-naive (n = 23), non-adherent (n = 42), and healthy control (n = 51) study groups. Serum levels of erythroferrone, hepcidin, and hephaestin were quantified using ELISA. Iron status and haemoglobinwere assessed using standard hematologic and biochemical methods. Logistic regression models were used to evaluate associations between biomarkerlevels, ART status, and IDA risk. ART non-adherence and ART-naivety were associated with significantly higher prevalence of IDA (65.4% and 50.0%, respectively) compared to ART adherence (17.6%, P =0.009). Erythroferrone levels were significantly suppressed in ART-naive and non-adherent individuals (median: 21.7 and 31.2 ng/mL, respectively) compared to adherent and healthy controls (38.1 and 50.2 ng/mL, P <0.0001). Elevated hepcidin levels were observed in ART-naive and non-adherent participants (113.0 and 84.1 ng/mL, respectively), aligning with functional iron deficiency. Hephaestin levels were markedly reduced in untreated and non-adherent groups, implicating impaired iron absorption. Binary logistic regression confirmed ART non-adherence (AOR = 9.97, 95% CI: 2.66–37.41), low erythroferrone (AOR = 0.094, 95% CI: 0.01–0.72), elevated hepcidin (AOR = 3.36, 95% CI: 1.36–8.25), and reduced hephaestin (AOR = 1.137 per μg/L decrease, 95% CI: 1.07–1.20) as independent predictors of IDA. ART status exerts a profound influence on iron homeostasis in PLWHIV through modulation of key regulatory proteins. Suppression of erythroferrone, elevation of hepcidin, and depletion of hephaestin underlie a triad of dysregulation that drives iron-restricted erythropoiesis. These findings callfor integrative diagnostic frameworks that include iron biomarkers beyond ferritin, and underscore the urgent need to address ART non-adherence as a modifiable determinant of haematologichealth in HIV.