A study of an Incidence of tuberculosis is linked to elevated hepcidin at HIV diagnosis

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Abstract

Background: Hepcidin prevents ferroportin-mediated iron efflux, which results in intracellular macrophage iron retention and may encourage Mycobacterium tuberculosis nutrient absorption and TB pathogenesis.

Aims & Objectives: In order to research into the relationship between incident pulmonary and extrapulmonary TB and plasma hepcidin levels, a retrospective cohort of HIV-positive, antiretroviral-native individuals had their plasma hepcidin levels tested at HIV diagnosis.

Methods & Materials: Between 5 August 2017 and 1 June 2019, 140 individuals were monitored, and 34 incident TB cases were found.

Discussion: After a median time to TB of 7 months, higher hepcidin was linked to a significantly increased chance of TB.

Conclusion: The need for time-sensitive biomarkers that can detect individual variations in TB risk and the elucidation of iron-related causative pathways cannot be overstated.

Keywords
biomarker, iron, nutrition, inflammation, mechanisms, time-sensitive

INTRODUCTION

Due to the different disease onset times, TB risk factors can be difficult to identify. Hepcidin, a tiny liver-derived peptide that encourages degradation of the intracellular inorganic iron exporter ferroportin, may also be involved in hostpathogen iron homeostasis, which has previously been linked to it. 1 Pro-inflammatory cytokines promote expression, which prevents intestinal enterocytes and macrophages from releasing iron. Hepcidin may facilitate conditions favourable to Mycobacterium TB by impacting human iron homeostasis. The objective of the current study was to examine, using a retrospective analysis of a longitudinal cohort, the link between hepcidin and susceptibility to tuberculosis (TB).
Stata Corp, College Station, Texas, USA) and Poisson regression, using incident TB (all TB) as the primary outcome. Associations were reported as incidence rate ratios (IRR). Sex and baseline ACT, absolute CD4 cell count, HIV type, age, and body mass index were a priori variables that were taken into account (BMI).

RESULTS

From 149 participants who were followed for 496 person-years (median follow-up, 1.8 years, interquartile range [IQR] 1.3–2.3), incident TB cases (n=34) were found. A median of 0.5 years passed before TB was diagnosed (IQR 0.3–1.1). Hepcidin (median 22.1 ng/ml, IQR 3.3-85.9), CD4 (median 250 cells/ll, IQR 91-502), age (34.4 years, 6 SD 10.3), haemoglobin (10.5 g/dl, 6 SD 2.3), ACT (0.49 g/l, 6 SD 0.27), and BMI (19.9 kg/m2, 6 SD 4.3) were baseline variables that did not statistically differ between incident TB cases Hepcidin and the risk of incident TB showed a dose-response relationship with a potential threshold impact (Figure 1). The chance of contracting TB was highest in the higher hepcidin quartile, which also accounted for.40% of all incident TB cases. The incidence of TB increased by two times when the top hepcidin quartile was compared to the combined lowest three quartiles (unadjusted IRR 2.05, 95% confidence interval [CI] 1.01-4.16). Both the unadjusted and adjusted hepcidin models showed similar magnitude and directional relationships; however, only the model with hepcidin adjusted for HIV type was statistically significant (adjusted IRR 2.10, 95%CI 1.03-4.26). Lower BMI, HIV-1, and factors previously thought to signify increased immunosuppression or inflammation were all related with a non-statistically significantly higher likelihood of developing tuberculosis in unadjusted models.

DISCUSSION

Our capacity to look at the temporal relationship between hepcidin as a risk factor for TB susceptibility rather than TB prognosis is a distinctive strength of this work. According to these findings, a higher hepcidin concentration is linked to a noticeably higher chance of contracting tuberculosis (TB) in those who have HIV. According to a recent publication from Indonesia, median hepcidin concentrations at cohort entry were likewise considerably higher among 45 incident TB patients when compared to controls who were HIV-infected [3], but this was only true for cases discovered between 31 and 60 days after cohort membership. Our results show, using a different statistical technique, that the window may be longer because baseline hepcidin was related to incident TB detected, on average, six months after enrollment. Together, these results show that increased hepcidin may be a proxy biomarker for subclinical TB, even if it is most likely a component of a complex multi-parameter risk profile with the pertinent time period still to be determined.

Hepcidin and incidence TB in HIV infection may be related, however the exact processes behind this link are unknown. Hepcidin seems to fit into a larger picture of inflammatory iron redistribution that this group has previously described using a bigger subset of the same cohort individuals. This image includes haemoglobin, plasma iron, ferritin, soluble transferrin receptor, and transferrin. [4] Infection-related host iron homeostasis is significantly regulated by hepcidin, and pathogen iron homeostasis, including both iron acquisition and storage, affects TB pathogenesis. [5–8] The host iron environment is altered by increased hepcidin in a way that favours MTB. The cause of tuberculosis is uncertain. Intriguingly, mounting evidence contends that M. tuberculosis may alter host cells hepcidin synthesis in order to foster an environment that is iron-friendly for the disease. If so, expanding current studies on hepcidin antagonists [10] to include hepcidin antagonists in TB prophylaxis or enhancing current anti-tuberculosis treatments may be necessary.

CONCLUSION

In conclusion, the likelihood of having TB and HIV co-infection increases with higher hepcidin concentrations upon HIV diagnosis. Understanding how hepcidin, host-pathogen iron homeostasis, immune activation/inflammation, and TB pathogenesis are related may help clinicians make evidence-based decisions when treating patients who are at high risk of developing TB and iron deficiency anaemia, two serious health
issues that are prevalent throughout much of the developing world. Overall, this study adds to the body of knowledge about who is most likely to develop clinical TB and the challenges that must be overcome when an individual’s TB management and population-level TB control are compromised by the transition from an infected-stable state to an infected-progressing state.

REFERENCES