Anaemia, iron deficiency and infections: new perceptions of the interaction between hepcidin, iron biomarkers, anaemia and inflammation in Malawian children

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Chapter three | Ancylostoma duodenale, severe anaemia and iron deficiency

![Figure 1. PCR-detected hookworm infection and its association with severe anaemia](image)

Displayed are the adjusted Odds Ratios and 95% confidence intervals for hookworm infection and its association with severe anaemia. Hookworm infection is defined as an *A. duodenale* and/or a *N. americanus* infection; infection load is defined by the following cycle thresholds (Ct): low 35<Ct<50; moderate 25<Ct≤35; high Ct≤25. In case of dual infection the lowest Ct-value was counted. Severe anaemia is defined as haemoglobin <5.0 g per decilitre. The multivariate model was adjusted for age, sex, recent use of haematinics or anti-malarial treatment, history of transfusions, death of a parent, limited maternal education (mother did not attend secondary school), wasting (defined as a Z-score of weight for height < -2), vitamin B12 deficiency (< 20 ng /dL), vitamin A deficiency (< 20 ng /dL), HIV, Epstein-Barr virus, bacteraemia, malaria parasitaemia, G6PD deficiency and IL-10-23 mutations.
Figure 2. PCR-detected hookworm infection and its association with iron deficiency
Displayed are the adjusted Odds Ratios and 95% confidence intervals for hookworm infection and its association with iron deficiency. Hookworm infection is defined as an *A. duodenale* and/or *A. americanus* infection; infection load is defined by the following cycle thresholds (Ct): low 35<Ct<50; moderate 25<Ct≤35; high Ct≤25. In case of dual infection the lowest Ct-value was counted. Iron deficiency is defined as a bone marrow smear score of 0 or 1 iron containing particles. The multivariate model was adjusted for age, sex, study location, HIV (human immunodeficiency virus) infection and wasting (defined as a Z-score of weight for height < -2). These analyses include only children with severe anaemia.
Figure 1. Univariate and multivariate linear regression analyses with all relevant covariates predicting log hepcidin. Regression coefficients are presented with 95% confidence interval. Bone marrow iron stores was scored in a range from 0 to 64. CRP: c-reactive protein; IL-6: interleukin 6. Bacteraemia was analyzed as dichotomous variable. Malaria was defined as a positive blood slide with concurrent fever (axillary temp >37.5°C), or history of fever within the previous 48 hours.

Figure 2. Univariate and multivariate logistic regression analyses with all relevant covariates predicting erythroblast iron incorporation. Regression coefficients are presented with 95% confidence interval. Insufficient erythroblast iron incorporation was defined as less than 30% erythroblasts having visible iron granules while having replete iron stores25. CRP: c-reactive protein. Previous use of haematinics is defined as use of iron supplements in the previous four weeks.
Chapter six | Hepcidin levels in severely anaemic children

Figure 3. Structural equation model for hepcidin, hypoxia/erythropoiesis, iron status and inflammation. In this exploratory model of the factors associated with serum hepcidin, the sizes of the associations are indicated by the standardized regression coefficients. An inverse association is indicated by a red line. This model was created containing all possible associations between the displayed variables, after which all non-significant arrows (p ≥0.05) were removed. A few non-significant correlations, deemed relevant by the authors, were retained in the figure, displayed as dashed arrows. C-reactive protein (CRP) was adjusted for malaria and bacteraemia; interleukin 6 (IL-6) was adjusted for bacteraemia (omitted for clarity). Iron in stores was defined as bone marrow iron score (0-6) 21. Insufficient erythrocyte iron incorporation was defined as less than 30% erythroblasts having visible iron granules while having replete iron stores. Erythroblast iron was defined as >30% of the erythroblasts having visible iron granules while having replete bone marrow iron stores 25. Alternative analyses without any non-significant arrow resulted in a virtually identical mode. The overall root mean square area of approximation, an indicator for model fit, was 0.288 (95% CI 0.272-0.304).

Chapter seven | Peripheral blood iron markers compared against bone marrow

Figure 1. Receiver operating characteristic curves of all iron makers with an AUCROC >0.500 (sTfR, ferritin, sTfR-F, hepcidin and MCV) in the identification of bone marrow iron stores deficiency.