Anaemia, iron deficiency and infections: new perceptions of the interaction between hepcidin, iron biomarkers, anaemia and inflammation in Malawian children
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Colour section
Figure 1. PCR-detected hookworm infection and its association with severe anaemia

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. 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.
Chapter three  |  Ancylostoma duodenedale, severe anaemia and iron deficiency

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. duodenedale 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. 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 6. 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 stores. 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

![Diagram of structural equation model for hepcidin, hypoxia/erythropoiesis, iron status and inflammation.](image)

**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) 24. 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 model. 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

![Graph of receiver operating characteristic curves of iron markers.](image)

**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.