**Supplemental Table S1: Definitions**

| Variable | Definition |
|---|---|
| *Infections* | The following are supplemental materials and will be published online only |
| Bacteremia | At least one bacterium isolated in blood (excluding common contaminants) |
| Clinical malaria | *P. falciparum* infection plus fever or history of fever in the preceding 24 hours |
| *Plasmodium falciparum* infection | Presence of asexual parasites in blood by microscopy or qPCR |
| Submicroscopic *Plasmodium falciparum* infection | Detection of parasites by qPCR and a negative blood smear |
| Hyperparasitemic *Plasmodium falciparum* infection | More than 100,000 parasites/µl of blood |
| Bone marrow microscopically negative for *P. falciparum* | Absence of *P. falciparum* parasites after the examination of 100 fields at 100x magnification |
| Positive Epstein Barr viral load | Detection of the virus in blood by real time qPCR (quantitative polymerase chain reaction) |
| Epstein Barr virus acute infection | Positive Epstein Barr viral load and IgM anti-antigen capsid virus (ACV) positive or IgM ACV negative and IgG ACV negative |
| Epstein Barr virus reactivation | Positive Epstein Barr viral load and the presence of IgG anti-ACV in the absence of IgM anti-ACV |
| Parvovirus B19 infection | Detection of the virus in blood by real-time qPCR |
| *Malnutrition* | |
| Stunting | Height-for-age Z-score (HAZ) <-2 standard deviations (SD) considering severe if Z scores were <-3 and moderate between <-2 SD and -3 SD. [1] |
| Underweight | Weight-for-age Z score (WAZ) <-2 SD, considering severe if Z scores were <-3 and moderate between <-2 SD and -3 SD. [1] |
| Wasting | Weight-for-height/length Z-score (WHZ) of <-2 SD, considering severe if Z scores were <-3 and moderate between <-2 SD and -3 SD[1] |
| Albumin deficiency | Albumin levels <34 g/l (laboratory reference value) |
| Prealbumin deficiency | Prealbumin levels <0.142 g/l in children <6 months of age, <0.120 g/l in children 6-12 months of age and <0.108 g/l in children 13-59 months of age [2] |
| Folate deficiency | Folate levels <3 ng/ml (laboratory reference value) |
| Vitamin A deficiency | Vitamin A levels <20 µg/dl [3] |
| Vitamin B12 deficiency | Vitamin B12 levels <200 pg/ml [4] |
| Iron deficiency by bone marrow | Categories 0 and 1 determined semi-quantitatively by the Perls' Prussian blue method [5] |

| | results |
|---|---|
| Iron deficiency by TfR-F (soluble transferrin receptor-ferritin) index | The ratio of soluble transferrin receptor to log ferritin >1.5 if C-Reactive Protein <1 mg/dl, and >0.8 if C-Reactive Protein ≥1 mg/dl [6] |
| *Markers of anemia pathophysiology* | |
| Blood loss in feces | Presence of blood in feces determined by Hemovcult® Single Slides for rapid test from BECKMAN COULTER (Brea, California, USA) |
| Blood loss in urine | Presence of blood in urine determine by Rapid test strips from NELISCO INC (Raleing, North Carolina, USA) |
| Dyserythropoiesis | Presence of erythroblasts with bi and tri-nuclearity, inter-nuclear chromatin bridges, nuclear pyknosis or any other chromatin alterations [7] |
| Hemolysis | Haptoglobin <0.32 g/l and lactate dehydrogenase (LDH) ≥975 U/l in children <7 months of age; LDH ≥1100 U/l in children 7-11 months of age; LDH ≥850 U/l in children 12-47 months of age; and LDH ≥615 U/l in children 48-59 months of age [8] |
| Reticulocyte Production Index <2 | RPI = reticulocyte index (RI)/maturation factor (MF), where RI = (reticulocyte count [%] × hematocrit [Hct]/0.36) and MF = b+(m)(x), where b = 1, m = 0.05, and x = (average normal population Hct − patient's Hct) [9] |
| *Erythropoiesis measures* | |
| % Erythroid cells (Morphology) normalized to degree of anemia* | Morphological quantification of erythropoiesis was the combined percentage of pro-erythroblasts and erythroblasts percentages counted in 100 nucleated cells from two bone marrow smears fixed and stained with May-Grünwald Eosin Methylene and 10% Giemsa. Z-scores of this measure of erythropoiesis relative to hemoglobin were calculated as multiples of the SD relative to a fitted cubic smoothing spline. |
| % Erythroid cells (Flow Cytometry) normalized to degree of anemia* | A flow-cytometric staining method used to track human erythroid differentiation *in vitro* by CD71 and CD235a expression[10] was applied directly *ex vivo* to bone marrow aspirates. Whole bone marrow was stained with fluorescein isothiocyanate-labeled anti-glycophorin A (BD Biosciences, clone GA-R2 (HIR2)) and phycoerythrin-labeled anti-CD71 (BD Biosciences, clone M-A712). After acquired acquiring 200.000 events per sample, a gate enriched for erythroblasts and reticulocytes was set with a gating method using equivalent mouse cell surface markers[11]. Z-scores of the decadic logarithm of this erythropoiesis gate relative to hemoglobin were [12]calculated as multiples of the SD relative to a fitted cubic smoothing spline. |
| Transcriptional score of | Genes differentially expressed by *in vitro* generated human erythroblasts as compared to |

| erythropoiesis normalized to degree of anemia* | other bone marrow lineages were identified from three publications[13-15]. Transcriptional erythropoiesis scores were calculated from the weighted averaged expression levels of these genes. Z-scores of erythropoiesis relative to hemoglobin was calculated as multiples of the SD relative to a fitted cubic smoothing spline. |
|---|---|

\* The adequacy of erythropoiesis can only be assessed when viewed in the context of hemoglobin level, as erythropoiesis levels increase dramatically in response to anemia. Therefore, erythropoiesis levels were normalized to hemoglobin levels to assess the physiological adequacy of the response. Using the normalized z-scores allows comparisons within the cohort. The morphological, flow-cytometric and transcriptional measures of erythropoiesis were broadly comparable in this study.

**References:**

1.     CDC. Centers for Disease Control and Prevention Clinical Growth Charts. *Available at:*

       *http://wwwcdcgov/growthcharts/clinical_chartshtm.*

2.     Nicholson JF, Pesce MA. Pruebas de laboratorio: Valores de referencia. *Nelson Textbook of Pediatrics.* Vol I. 17th ed.

       Madrid: Elsevier España; 2004:2396-2426.

3.     Sanjoaquin MA, Molyneux ME. Malaria and vitamin A deficiency in African children: a vicious circle? *Malaria journal.*

       2009;8:134.

4.     Selhub J, Jacques PF, Dallal G, Choumenkovitch S, Rogers G. The use of blood concentrations of vitamins and their

       respective functional indicators to define folate and vitamin B12 status. *Food and nutrition bulletin.* Jun 2008;29(2

       Suppl):S67-73.

5.     Beutler E, Robson MJ, Buttenwieser E. A comparison of the plasma iron, iron-binding capacity, sternal marrow iron and

       other methods in the clinical evaluation of iron, stores. *Ann Intern Med.* Jan 1958;48(1):60-82.

6.     Aguilar R, Moraleda C, Quinto L, et al. Challenges in the diagnosis of iron deficiency in children exposed to high

       prevalence of infections. *PloS one.* 2012;7(11):e50584.

7.     Wickramasinghe SN. Dyserythropoiesis and congenital dyserythropoietic anaemias. *Br J Haematol.* 1997;98(4):785-797.

8.     Heil W KR, Zawta B. . Reference Ranges for Adults and Children: Pre-Analytical Considerations. . *Mannheim,*

       *Germany, Roche Diagnostics, number 133.* 2000.

9.     Ouma C, Keller CC, Davenport GC, et al. A novel functional variant in the stem cell growth factor promoter protects

       against severe malarial anemia. *Infection and immunity.* Jan 2010;78(1):453-460.

10.    Loken MR, Shah VO, Dattilio KL, Civin CI. Flow cytometric analysis of human bone marrow: I. Normal erythroid

       development. *Blood.* 1987;69(1):255-263.

11.    Socolovsky M, Nam H, Fleming MD, Haase VH, Brugnara C, Lodish HF. Ineffective erythropoiesis in Stat5a(-/-)5b(-/-)

       mice due to decreased survival of early erythroblasts. *Blood.* 2001;98(12):3261-3273.

12.      Neurologic impairment in children associated with maternal dietary deficiency of cobalamin--Georgia, 2001. *MMWR Morb Mortal Wkly Rep.* 2003;52(4):61-64.

13.      Watkins NA, Gusnanto A, de Bono B, et al. A HaemAtlas: characterizing gene expression in differentiated human blood cells. *Blood.* 2009;113(19):e1-9. doi: 10.1182/blood-2008-1106-162958. Epub 162009 Feb 162919.

14.      Liu XL, Yuan JY, Zhang JW, Zhang XH, Wang RX. Differential gene expression in human hematopoietic stem cells specified toward erythroid, megakaryocytic, and granulocytic lineage. *J Leukoc Biol.* 2007;82(4):986-1002. Epub 2007 Jul 1012.

15.      Macaulay IC, Tijssen MR, Thijssen-Timmer DC, et al. Comparative gene expression profiling of in vitro differentiated megakaryocytes and erythroblasts identifies novel activatory and inhibitory platelet membrane proteins. *Blood.* 2007;109(8):3260-3269. Epub 2006 Dec 3227.

**Supplemental Table 2: Distribution of the study variables and anemia within HIV-groups**

| Variable | | Study group | | Total |
|---|---|---|---|---|
| | | **Controls** | **Cases** | |
| ID by TfR-F index according to CRP | HIV-negative | 101/242 (42%) | 184/262 (70%) | 285/504 (57%) |
| | HIV-positive | 4/4 (100%) | 47/72 (65%) | 51/76 (67%) |
| Parvovirus B19 infection | HIV-negative | 5/266 (2%) | 23/297 (8%) | 28/563 (5%) |
| | HIV-positive | 0/6 (0%) | 2/93 (2%) | 2 99 (2%) |
| Positive EBV viral load | HIV-negative | 36/265 (14%) | 61/296 (21%) | 97/561 (17%) |
| | HIV-positive | 0/6 (0%) | 42/93 (45%) | 42/99 (42%) |
| EBV acute infection | HIV-negative | 5/258 (2%) | 14/284 (5%) | 19/542 (4%) |
| | HIV-positive | 0/6 (0%) | 8/85 (9%) | 8/91 (9%) |
| EBV reactivation | HIV-negative | 24/258 (9%) | 35/284 (12%) | 59/542 (11%) |
| | HIV-positive | 0/6 (0%) | 26/85 (31%) | 26/91 (29%) |
| Wasting (WHZ < -2 SD) | HIV-negative | 17/259 (7%) | 66/293 (23%) | 83/552 (15%) |
| | HIV-positive | 1/6 (17%) | 56/93 (60%) | 57/99 (58%) |
| Stunting (HAZ < -2 SD) | HIV-negative | 34/262 (13%) | 77/293 (26%) | 111/555 (20%) |
| | HIV-positive | 0/6 (0%) | 52/93 (56%) | 52/99 (53%) |
| Underweight (WAZ <-2 SD) | HIV-negative | 29/263 (11%) | 114/297 (38%) | 143/560 (26%) |
| | HIV-positive | 1/6 (17%) | 67/93 (72%) | 68/99 (69%) |
| Severe wasting (WHZ <-SD) | HIV-negative | 8/259 (3%) | 28/293 (10%) | 36/552 (7%) |
| | HIV-positive | 0/6 (0%) | 39/93 (42%) | 39/99 (39%) |
| Severe stunting (HAZ <-3 SD) | HIV-negative | 12/262 (5%) | 19/293 (6%) | 31/555 (6%) |
| | HIV-positive | 0/6 (0%) | 35/93 (38%) | 35/99 (35%) |
| Severe underweight (WAZ <-3 SD) | HIV-negative | 12/263 (5%) | 56/297 (19%) | 68/560 (12%) |
| | HIV-positive | 1/6 (17%) | 53/93 (57%) | 54/99 (55%) |
| Albumin deficiency | HIV-negative | 10/262 (4%) | 104/293 (35%) | 114/555 (21%) |
| | HIV-positive | 0/5 (0%) | 53/87 (61%) | 53/92 (58%) |
| Prealbumin deficiency | HIV-negative | 90/260 (35%) | 265/292 (91%) | 355/552 (64%) |
| | HIV-positive | 2/5 (40%) | 77/86 (90%) | 79/91 (87%) |
| Folate deficiency | HIV-negative | 0/236 (0%) | 0/261 (0%) | 0/497 (0%) |
| | HIV-positive | 0/4 (0%) | 0/72 (0%) | 0/76 (0%) |

| | | | | |
|---|---|---|---|---|
| Vitamin A deficiency | HIV-negative | 74/263 (28%) | 205/294 (70%) | 279/557 (50%) |
| | HIV-positive | 2/5 (40%) | 59/88 (67%) | 61/93 (66%) |
| Vitamin B12 deficiency | HIV-negative | 50/249 (20%) | 50/283 (18%) | 100/532 (19%) |
| | HIV-positive | 1/5 (20%) | 11/80 (14%) | 12/85 (14%) |
| Bacteremia | HIV-negative | 3/264 (1%) | 17/287 (6%) | 20/551 (4%) |
| | HIV-positive | 0/6 (0%) | 14/93 (15%) | 14/99 (14%) |
| *Pf.* infection | HIV-negative | 19/266 (7%) | 137/286 (48%) | 156/552 (28%) |
| | HIV-positive | 0/6 (0%) | 19/90 (21%) | 19/96 (20%) |
| Hyperparasitemic *Pf.* | HIV-negative | 0/266 (0%) | 27/286 (9%) | 27/552 (5%) |
| | HIV-positive | 0/6 (0%) | 5/90 (6%) | 5/96 (5%) |
| Submicroscopic *Pf.* | HIV-negative | 11/263 (4%) | 25/204 (12%) | 36/467 (8%) |
| | HIV-positive | 0/6 (0%) | 10/83 (12%) | 10/89 (11%) |
| Hookworm infection | HIV-negative | 10/146 (7%) | 4/133 (3%) | 14/279 (5%) |
| | HIV-positive | 0/2 (0%) | 1/51 (2%) | 1/53 (2%) |

**Abbreviations**: ID: iron deficiency; TfR-F index: ratio of soluble transferrin receptor to log ferritin; CRP: C-reactive protein;

EBV: Epstein-Barr virus; WHZ: weight-for-height/length Z-score; HAZ: height-for-age Z-score; WAZ: weight-for-age Z score;

*Pf: P. falciparum*.