Nutritional Status of Young Children with Inherited Blood Disorders in Western Kenya

Becky L. Tsang, Kevin M. Sullivan, Laird J. Ruth, Thomas N. Williams, and Parminder S. Suchdev*

Hubert Department of Global Health, Rollins School of Public Health and Department of Pediatrics, School of Medicine, Emory University, Atlanta, Georgia; Nutrition Branch, Centers for Disease Control and Prevention, Atlanta, Georgia; Centre for Geographic Medicine Research-Coast, Kenya Medical Research Institute, Kilifi, Kenya; Nuffield Department of Clinical Medicine, Oxford, United Kingdom

Abstract. To determine the association between a range of inherited blood disorders and indicators of poor nutrition, we analyzed data from a population-based, cross-sectional survey of 882 children 6–35 months of age in western Kenya. Of children with valid measurements, 71.7% were anemic (hemoglobin < 11 g/dL), 19.1% had ferritin levels < 12 μg/L, and 30.9% had retinol binding protein (RBP) levels < 0.7 μmol/L. Unadjusted analyses showed that compared with normal children, homozygous α-thalassemia individuals had a higher prevalence of anemia (82.3% versus 66.8%, P = 0.001), but a lower prevalence of low RBP (20.5% versus 31.4%, P = 0.024). In multivariable analysis, homozygous α-thalassemia remained associated with anemia (adjusted odds ratio [aOR] = 1.8, P = 0.004) but not with low RBP (aOR = 0.6, P = 0.065). Among young Kenyan children, α-thalassemia is associated with anemia, whereas G6PD deficiency, haptoglobin 2-2, and HbS are not; none of these blood disorders are associated with iron deficiency, vitamin A deficiency, or poor growth.

INTRODUCTION

A high percentage of young children in Kenya have inherited blood disorders. Among the most common in this region are α-thalassemia, sickle cell hemoglobin (HbS), glucose-6-phosphate dehydrogenase (G6PD) deficiency, and haptoglobin (Hp) 2-2. A high prevalence of all of these disorders have been shown previously in Kenya and elsewhere in sub-Saharan Africa, with heterozygous α-thalassemia (–α/αα) and homozygous (–α/αα) α-thalassemia estimated at 39% and 15%, respectively, in coastal Kilifi, sickle cell trait (HbAS) prevalence estimated at 15–28%, G6PD deficiency estimated as high as 20%, and Hp 2-2 estimated as high as 25%. All four blood disorders are associated with adverse health outcomes with varying severity and potential effect on nutrition status. Individuals with α-thalassemia are largely asymptomatic, but experience chronic mild anemia. HbAS is generally regarded as a benign condition, whereas sickle cell anemia (HbSS) is associated with chronic ill health and reduced life expectancy. Individuals with G6PD deficiency are more susceptible to hemolytic anemia triggered by certain drugs or foods. Inheritance of the Hp 2-2 genotype is not a blood disorder per se, but because the protein is active in iron metabolism, it may have a role in anemia.

The relationships between these four blood disorders and risk for anemia and malaria are multifaceted and have the potential to confound the interpretation of nutrition indicator outcomes if not taken into consideration. On one hand they may modify the risk of anemia and chronic malnutrition through reduced risk of severe malaria, the other hand some inherited blood disorders (including α-thalassemia and HbSS) can have a negative impact on hemoglobin concentration and subsequent growth. For example, studies have linked HbSS with growth retardation and an increase in macronutrient requirements, whereas the prevalence of stunting was reported to be lower among young HbAS children who experienced malaria episodes in Ghana than among HbAA children. Despite the potential for direct and indirect effects of anemia and malaria infection on growth and nutrition indicators, the relationships between inherited blood disorders and the overall nutritional status of young children are not well known. The confounding effects of inherited blood disorders are rarely considered in studies of nutrition in areas where inherited blood disorders are widespread.

Our purpose in this study was to investigate the relationship between each of four inherited blood disorders (Hp 2-2, G6PD deficiency, HbAS/HbSS, and the α-thalassemia genotypes [–α/αα, –α/αα]) and the prevalence of six conditions associated with poor nutrition (anemia, iron deficiency, vitamin A deficiency, VAD, stunting, wasting, and underweight) among preschool children in western Kenya.

METHODS

Study setting and design. We used data from a population-based, cross-sectional survey of children who participated in the Nyando Integrated Child Health and Education Project (NICHE), a cluster randomized trial that evaluated the effectiveness of the promotion and sale of health products, including micronutrient powders, in 60 study villages during 2007–2010. A complete description of NICHE, including the study sampling methodology and results, are provided elsewhere.

In brief, the survey was conducted in rural Nyando Division in Nyanza Province, western Kenya, where the population is of the Luo ethno-linguistic group and where the main occupation is subsistence farming; previously collected data from the NICHE project indicated a high rate of morbidity from malaria and poor nutrition among residents of this area. In 2007, researchers used the 1999 Nyando District census as a reference to select 30 intervention villages and 30 comparison villages for participation in the survey, with the probability of a village’s selection proportional to its size. An updated household census was conducted before the August 2010 survey, and 19 compounds per village were randomly selected. All children 6–35 months of age from each compound were eligible for inclusion in the survey. Of 1,079 age-eligible
children, we included 861 in our analyses of survey data (Figure 1); however, because of inadequate blood samples from some children, we did not include all 861 in all analyses. Field staff used birth certificates or immunization records to verify the ages of all children in the survey.

Assessment of children’s nutritional status, hemoglobin genotype, and socioeconomic status. Field workers administered a questionnaire to a parent or other primary caretaker of participating children to collect information on the children’s age, sex, illness status, and use of micronutrient supplementation. The questionnaire was written in English, translated into the local Dholuo language, and back-translated into English to verify the accuracy of the original translation. Caretakers were asked to report whether children had experienced diarrhea, respiratory disease, or fever within the preceding 24 hours, and clinical malaria was diagnosed on the basis of a positive malaria blood smear in conjunction with a report of fever in the preceding 24 hours. The survey also collected data on multiple indicators of socioeconomic status (SES), including maternal education, household assets, and infrastructure.

Trained anthropometrists measured the recumbent length of children < 24 months of age and the standing height of those ≥ 24 months of age to the nearest 0.1 cm using a wooden measuring board (Irwin Shorr Productions, Olney, MD) and measured children’s weight to the nearest 0.1 kg using a digital scale (Seca Corp., Hanover, MD). We defined stunting, underweight, and wasting as, respectively, a height-for-age z-score (HAZ), a weight-for-age z-score (WAZ), and a weight-for-height z-score (WHZ) less than two standard deviations below the mean values for these scores based on international growth standard data.21

Capillary blood was used for all hematological analyses. After wiping the first drop of blood, field workers measured the hemoglobin (Hb) concentration in the second drop using a HemoCue B-Hemoglobin device (Angelholm, Sweden), collected 400–500 μL of blood in heparinized microcontainers, and made Giemsa-stained thick blood films. Microcontainers of collected blood were stored in cold boxes during the day until centrifugation each evening.

Anemia was defined as an Hb concentration < 11.0 g/dL;22 because all study villages were at elevations below 1,000 m, we did not apply an altitude correction. Collected blood samples were analyzed at the Kenyan Medical Research Institute (KEMRI)/Centers for Disease Control and Prevention (CDC) laboratory in Kisian, Kenya to determine whether malaria parasitemia were present and, if so, in what quantity. Children with severe anemia (Hb levels < 7.0 g/dL) or clinically diagnosed malaria were referred to the nearest hospital or clinic for follow-up. Ferritin, C-reactive protein (CRP), transferrin receptor (TIR), α-1-acid glycoprotein (AGP), and retinol binding protein (RBP) were analyzed using a sandwich enzyme-linked immunosorbent assay (ELISA) technique (VitA-Iron Laboratory, Germany).23 Low ferritin was defined as a plasma ferritin concentration < 12 μg/L,24,25 and iron deficiency was defined as low ferritin in the absence of inflammation (a CRP level ≤ 5 mg/L and an AGP level ≤ 1 g/L).26 Although TIR data were collected, we did not include it in this analysis because of the potential effect of malaria, inflammation, and hemoglobinopathies on TIR levels.27 We defined low RBP as < 0.7 μmol/L28 and VAD as low RBP with no inflammation.

β-globin genotyping for the HbA and HbS alleles and the 3.7-kilobase α-globin chain deletion (the most common African form of α-thalassemia) and the Hb types were determined by polymerase chain reaction (PCR) as described in detail previously.10,29–31 On the basis of results from recent phenotypic studies (Shivang Shah, unpublished data), we classified males as G6PD-deficient if they were hemizygous for the G6PD− allele and females as G6PD-deficient if they were either homozygous for the G6PD− allele or heterozygous for both the G6PD− and G6PD+ alleles.29,32 All genetic analyses were conducted at the KEMRI-Wellcome Trust laboratory in Kilifi, Kenya; details of all analyses are available elsewhere.17,30,31

Iron supplementation and Sprinkles (a micronutrient powder) use were also assessed in the survey. The Sprinkles formulation used in this area included 14 micronutrients, including 12.5 mg of iron as microencapsulated ferrous fumarate and 375 μg of vitamin A.33 SES was categorized in

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Figure 1. Selection of survey participants in Nyando Division, Kenya.
quintiles to relative poverty using a principal components
analysis (PCA) wealth index developed by the World Bank.34

Data synthesis. In our analyses, we categorized children
into two age groups: 6–23 months and 24–35 months to cap-
ture those within the critical nutrition period of < 24 months
compared with those 24 months and over.35 The Hb, ferritin,
and RBP levels were dichotomized using the cut-off points
defined previously because the primary objective was to
identify whether nutritional status at internationally accepted
definitions varied by blood disorder. Because only 30 children
were classified as wasted, we did not include wasting as a
covariate in logistic regression.

Statistical analysis. We used the Rao-Scott \( \chi^2 \) test36 to iden-
tify crude associations between the blood disorders (primary
exposure) and other variables. We then used logistic regres-
sion analysis to assess the relationship between each blood
disorder and any nutrition outcome (anemia, low ferritin,
low RBP, stunting, wasting, and underweight) shown to be
statistically significant (\( \chi^2 P < 0.05 \)). The HbAA children
served as the reference for those with HbAS, normal (aa/aa)
genotype or heterozygote (–a/aa) children for \( \alpha^-\)-thalassemia
homozygote children (–a/–a); children with normal G6PD
levels for those with G6PD deficiency, and children with the
Hp 1-1/Hp 2-1 genotype served as the reference group in
analyses for Hp 2-2. Because only 14 children carried the
HbSS genotype, we did not include these children in the logistic
regression analysis.

In multivariable models, acute and chronic inflammation
were accounted for by controlling for both CRP and AGP in
the adjusted model.26 We also assessed for interaction and
confounding of covariates identified in previous studies,
including male sex, low SES (defined as the bottom three
PCA quintiles), illness (diarrhea, respiratory illness, or fever)
within the preceding 24 hours, child-feeding practices in the
preceding 24 hours (breastfeeding, tea consumption, iron sup-
plementation, use of Sprinkles, dirt/earth consumption [a form
of pica behavior]), inflammation (elevated CRP and/or AGP),
and malaria status. To account for co-inheritance of blood
disorders and co-existing health conditions, we also included
nutrition outcomes and blood disorders as covariates in initial
models. Blood disorders were retained in final models regard-
less of \( P \) value.

We included covariates in our full logistic regression model
if results of our bivariate analysis indicated there was a signif-
ificant association with a blood disorder (\( P < 0.05 \)), if the inter-
action between the primary exposure and covariate was
significant (\( P < 0.05 \)), or if they changed the odds ratio (OR)
for the relationship between the primary exposure and the
covariate by more than 10%. We conducted backward regres-
sion first for any interaction terms and then by removing
variables that were not confounders or independent predic-
tors of the outcome. At each step, we monitored the OR for
the relationship between the primary exposure and the covari-
te to ensure that removal of a covariate did not result in
confounding. However, we kept age, sex, and all other blood
disorders in the model as potential confounding covariates
regardless of the \( P \) value for their relationship with a blood
disorder of interest. We used the same process for all signifi-
cant associations between blood disorders and indicators of
poor nutrition. We defined collinearity between covariates as
condition indices (CI) > 30 using a SAS collinearity macro37 in
the final models. Final models included all remaining signifi-
cant two-way interactions, statistically significant independent
variables, and confounding variables as defined above.

Data were analyzed using SAS version 9.3 (SAS Institute
Inc., Cary, NC) taking into account the complex survey design
of 60 primary sampling units (villages) by using PROC
SURVEYFREQ and PROC SURVEYLOGISTIC. We con-
sidered results to be statistically significant if two-sided
\( P \) values were < 0.05.

Ethical considerations. The Scientific Steering Committee
and the Ethical Review Committee of KEMRI in Nairobi
and the CDC Institutional Review Board approved all
study protocols.

RESULTS

We classified 29.8% of children surveyed as stunted, 12.1%
as underweight, 3.5% as wasted, 19.1% as having low ferritin
levels, and 30.9% as having low RBP levels (Table 1). We
classified 59.4% as having one or more of the following geno-
types or conditions: Hp 2-2, G6PD deficiency, \( \alpha^-\)-thalassemia,

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics and health indicators of children aged 6–35 months in western Kenya, 2010*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sample size = 861</td>
<td>n/N</td>
</tr>
<tr>
<td>Sex, female</td>
<td>427/861</td>
</tr>
<tr>
<td>Age, 6–23 months</td>
<td>463/861</td>
</tr>
<tr>
<td>Child slept under bed next previous night</td>
<td>777/837</td>
</tr>
<tr>
<td>Inherited blood disorders</td>
<td></td>
</tr>
<tr>
<td>G6PD deficiency</td>
<td>56/829</td>
</tr>
<tr>
<td>Haptoglobin polymorphism, Hp 2-2</td>
<td>164/805</td>
</tr>
<tr>
<td>( \alpha^-)-Thalassemia</td>
<td></td>
</tr>
<tr>
<td>Heterozygotes (aa/–a)</td>
<td>319/826</td>
</tr>
<tr>
<td>Homozygotes (–a/–a)</td>
<td>79/826</td>
</tr>
<tr>
<td>Sickle cell hemoglobin</td>
<td></td>
</tr>
<tr>
<td>Trait (HbAS)</td>
<td>146/857</td>
</tr>
<tr>
<td>SCA (HbSS)</td>
<td>14/857</td>
</tr>
<tr>
<td>Nutrition status</td>
<td></td>
</tr>
<tr>
<td>Anemia (Hb &lt; 11 g/dL)</td>
<td>617/861</td>
</tr>
<tr>
<td>Plasma ferritin &lt; 12 μg/L†</td>
<td>162/850</td>
</tr>
<tr>
<td>Iron deficiency‡</td>
<td>124/333</td>
</tr>
<tr>
<td>Retinol binding protein &lt; 0.7 μmol/L†</td>
<td>263/850</td>
</tr>
<tr>
<td>Vitamin A deficiency‡</td>
<td>52/333</td>
</tr>
<tr>
<td>Inflammation</td>
<td></td>
</tr>
<tr>
<td>C-reactive protein &gt; 5.0 mg/L</td>
<td>292/850</td>
</tr>
<tr>
<td>( \alpha^-)/acid glycoprotein &gt; 1.0 g/L</td>
<td>518/850</td>
</tr>
<tr>
<td>Any inflammation (AGP &gt; 1.0 g/L or CRP &gt; 5.0 mg/L)</td>
<td>528/861</td>
</tr>
<tr>
<td>Anthropometry</td>
<td></td>
</tr>
<tr>
<td>Stunted (HAZ &lt; -2.0)</td>
<td>255/856</td>
</tr>
<tr>
<td>Underweight (WAZ &lt; -2.0)</td>
<td>104/859</td>
</tr>
<tr>
<td>Wasted (WHZ &lt; -2.0)</td>
<td>30/857</td>
</tr>
<tr>
<td>Nutrition practices</td>
<td></td>
</tr>
<tr>
<td>Sprinkles (in last 24 hr)</td>
<td>92/837</td>
</tr>
<tr>
<td>Iron supplementation (in last 24 hr)</td>
<td>58/839</td>
</tr>
<tr>
<td>Tca consumption (in last 24 hr)</td>
<td>692/832</td>
</tr>
<tr>
<td>Breast-feeding (in last 24 hr)</td>
<td>417/838</td>
</tr>
<tr>
<td>Self-reported pica (in last 24 hr)</td>
<td>382/800</td>
</tr>
<tr>
<td>Illness</td>
<td></td>
</tr>
<tr>
<td>Clinical malaria</td>
<td>124/857</td>
</tr>
<tr>
<td>Diarrhea (in last 24 hr)</td>
<td>203/836</td>
</tr>
<tr>
<td>Fever (in last 24 hr)</td>
<td>349/829</td>
</tr>
<tr>
<td>Respiratory (in last 24 hr)</td>
<td>319/839</td>
</tr>
</tbody>
</table>

*G6PD = glucose-6-phosphate dehydrogenase; SCA = sickle cell anemia; Hb = hemoglobin; HAZ = height-for-age z-score; WAZ = weight-for age z-score; AGP = \( \alpha^-\)-acid glycoprotein; CRP = C-reactive protein;
†Uncorrected for inflammation.
‡Excludes N = 517 children with elevated CRP and/or AGP.
or HbAS/HbSS. In the overall population, 38.6% were α+thalassemia heterozygotes, 9.6% α-thalassemia homozygotes, 20.4% had Hp 2-2, 17.0% had HbAS, 1.6% had HbSS, and 6.8% had G6PD deficiency; the prevalence of these genotypes and conditions did not differ significantly by sex (data not shown).

Anemia prevalence did not differ significantly by Hp subtype, HpS genotype, or G6PD deficiency status (Table 2). However, the prevalence of anemia did differ significantly by α+thalassemia strata (overall trend \( P = 0.003 \), not shown), with the prevalence being significantly higher among homozygotes compared with heterozygotes (\( P = 0.014 \)) or the normal genotype (\( P = 0.001 \)). Both heterozygotes and homozygotes were more likely to have anemia than those with normal genotype (crude ORs = 1.53 and 2.31, respectively, not shown).

We found no significant bivariate association between low ferritin levels and any of the blood disorders investigated. The prevalence of low RBP was significantly lower among children with homozygous α-thalassemia (\( P = 0.024 \)) compared with those with normal genotype; however, the prevalence of low RBP did not differ significantly between α-thalassemia heterozygous children and those with normal genotype (\( P = 0.600 \)). There was no significant relationship between low RBP status and any of the other blood disorders. After we removed children with any inflammation (\( N = 517; 60.8\% \) of the study population) from our analyses for VAD and iron deficiency, iron deficiency was not associated with any disorders and VAD was associated only with the heterozygous α-thalassemia genotype (\( P = 0.034 \), not shown). Given the high percentage of children excluded because of inflammation, we did not conduct a logistic regression analysis of the relationship between VAD (RBP < 0.7 µmol/L and no inflammation) and α-thalassemia.

Inflammation was not significantly associated with any of the inherited blood disorders; elevated CRP varied from 21.4–37.2%, whereas elevated AGP varied from 53.6–64.3% among the disorders (not shown). None of the inherited blood disorders were associated with the prevalence of stunting, wasting, or underweight.

### Relationship between homozygous α+thalassemia (α+/α+) and low RBP

After adjusting for significant covariates, multivariate logistic regression results showed no significant relationship between homozygosity for α+thalassemia and low RBP (aOR = 0.61, \( P = 0.065 \); 95% CI = 0.36–1.03) but did show low RBP to be associated with a greater prevalence of being underweight, having inflammation, and testing positive for malaria (Table 3). We retained age group in the regression model to control for any confounding as a result of survival bias, and we kept HbAS, Hp 2-2 and G6PD deficiency in the model as potential confounders because of co-inheritance of blood disorders. We found no evidence of significant collinearity among the independent variables.

### Relationship between α-thalassemia (α/aα, –α/–α) and anemia

After adjusting for significant covariates, α-thalassemia was still positively associated with anemia (\( P = 0.004 \)) (Table 4); children with α-thalassemia were significantly more likely to have anemia than those without (aOR = 1.78; 95% CI = 1.20–2.62). Other variables in the adjusted model associated with anemia were young age (6–23 months), low SES, male sex, low ferritin concentration, inflammation, and a positive malaria smear. Of these, a positive malaria smear (aOR = 6.81, 95% CI = 4.26–10.89), a low ferritin concentration (aOR = 4.43, 95% CI = 2.67–7.32), and inflammation (aOR = 3.24, 95% CI = 2.04–5.14) had the strongest associations with anemia. We kept HbAS, Hp 2-2, and G6PD deficiency in the model as potential confounders and found no evidence of significant collinearity among the covariates.

### DISCUSSION

Despite a high prevalence of both malnutrition and inherited blood disorders in this population, we found no significant
associations between the blood disorders and conditions indicative of poor nutrition, except for a positive association between α⁺-thalassemia and anemia, which has been found previously Kenya, Nigeria, and Cambodia population. Thus, our results suggest that α⁺-thalassemia should be considered when evaluating anemia etiology and the impact of anemia interventions. However, there may be limited value of the other measured blood disorders (G6PD deficiency, Hp 2-2, and HbAS) in interpreting cross-sectional nutrition surveys.

Although anemia prevalence differed by α⁺-thalassemia genotype, the prevalence of low ferritin levels did not. Our finding is consistent with a previous study among children on the coast of Kenya. It is well known that anemia prevalence in children with α⁺-thalassemia is associated with the disorder itself or another mechanism associated with the disorder, rather than with α⁺-thalassemia’s relationship to iron metabolism.

The relationship between α⁺-thalassemia and anemia is especially important in locations such as western Kenya where malaria is endemic and the prevalence of α⁺-thalassemia (48.2% overall) is high. Awareness of the underlying prevalence of blood disorders in a population may help program officials better interpret the impact of interventions to prevent and treat anemia. Impact evaluations of anemia prevention or treatment programs may not be a true reflection of program success because anemia attributable to α⁺-thalassemia will not be corrected. Though systematic screening for α⁺-thalassemia may be unrealistic in regions with limited resources, partial population sampling or understanding of the distribution of α⁺-thalassemia are potential tools that could be considered during monitoring and evaluation of anemia control programs.

We found a relatively high prevalence of low RBP and VAD across all blood disorder subgroups. We also found that low RBP status was associated with being underweight, having a positive malaria smear, and having elevated levels of inflammatory markers. Clinical trial results have shown that vitamin A supplementation can decrease the parasite load, but it is unclear if vitamin A supplementation has any

### Table 3
Factors associated with low RBP among young children aged 6–35 months in western Kenya, 2010* (N = 756)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted OR</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α⁺-Thalassemia: –a/–a (ref = αα/αα or –a/αα)</td>
<td>0.54†</td>
<td>0.61 (0.36–1.03)</td>
</tr>
<tr>
<td>Child demographics and characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 6–23 months (ref = 24–35 months)</td>
<td>0.98</td>
<td>1.12 (0.79–1.70)</td>
</tr>
<tr>
<td>Underweight (ref = WAZ ≥ -2)</td>
<td>2.30‡</td>
<td>1.96 (1.15–3.34)</td>
</tr>
<tr>
<td>Morbidity and infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation (ref = normal CRP and AGP)</td>
<td>4.97†</td>
<td>3.33 (2.14–5.18)</td>
</tr>
<tr>
<td>Positive malaria smear (ref = no malaria)</td>
<td>3.90‡</td>
<td>2.72 (1.91–3.87)</td>
</tr>
<tr>
<td>Blood disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G6PD deficiency (ref = normal)</td>
<td>0.74</td>
<td>0.84 (0.41–1.69)</td>
</tr>
<tr>
<td>HbAS (ref = HbAA)</td>
<td>0.86</td>
<td>1.05 (0.66–1.69)</td>
</tr>
<tr>
<td>Hp 2-2 (ref = Hp 1-1 and Hp 2-1)</td>
<td>1.34</td>
<td>1.41 (0.97–2.05)</td>
</tr>
</tbody>
</table>

RBP = retinol binding protein; WAZ = weight-for-age z score; Inflammation = CRP > 5 mg/L and/or AGP > 1 g/L; Normal AGP/CRP = CRP ≤ 5 mg/L, AGP ≤ 1 g/L; G6PD = glucose-6-phosphate-dehydrogenase; HbAS = sickle cell trait; Hp = haptoglobin. *Unadjusted odds ratio (OR) P < 0.05.

### Table 4
Factors associated with anemia among young children aged 6–35 months in western Kenya, 2010* (N = 739)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted OR</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α⁺-Thalassemia: –a/–a or –a/–a (ref = αa/αa)</td>
<td>1.65†</td>
<td>1.78 (1.20–2.62)</td>
</tr>
<tr>
<td>Child demographics and characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 6–23 months (ref = 24–35 months)</td>
<td>1.48†</td>
<td>1.35 (0.91–2.01)</td>
</tr>
<tr>
<td>Breastfeeding in the last 24 hours</td>
<td>1.54†</td>
<td>1.38 (0.94–2.05)</td>
</tr>
<tr>
<td>SES quintile 1–3 (ref = quintile 4–5)</td>
<td>1.44†</td>
<td>1.52 (1.06–2.19)</td>
</tr>
<tr>
<td>Male (ref = female)</td>
<td>1.51†</td>
<td>1.66 (1.06–2.59)</td>
</tr>
<tr>
<td>Underweight (ref = WAZ ≥ -2)</td>
<td>2.20†</td>
<td>1.85 (1.02–3.34)</td>
</tr>
<tr>
<td>Morbidity and infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low iron (ref = ferritin ≥ 12 μg/L)</td>
<td>1.79†</td>
<td>4.43 (2.67–7.32)</td>
</tr>
<tr>
<td>Inflammation (ref = normal CRP &amp; AGP)</td>
<td>3.43†</td>
<td>3.24 (2.04–5.14)</td>
</tr>
<tr>
<td>Positive malaria smear (ref = no malaria)</td>
<td>5.79†</td>
<td>6.81 (4.26–10.89)</td>
</tr>
<tr>
<td>Blood disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G6PD deficiency (ref = normal)</td>
<td>1.01</td>
<td>1.01 (0.45–2.31)</td>
</tr>
<tr>
<td>HbAS (ref = HbAA)</td>
<td>0.47</td>
<td>0.69 (0.41–1.16)</td>
</tr>
<tr>
<td>Hp 2-2 (ref = Hp 1-1 or Hp 2-1)</td>
<td>1.23</td>
<td>0.97 (0.63–1.50)</td>
</tr>
</tbody>
</table>

SES = socioeconomic status; WAZ = weight-for-age z score; Inflammation = CRP > 5 mg/L and/or AGP > 1 g/L; Normal AGP/CRP = CRP ≤ 5 mg/L, AGP ≤ 1 g/L; G6PD = glucose-6-phosphate-dehydrogenase; HbAS = sickle cell trait; Hp = haptoglobin. *Unadjusted odds ratio (OR) P < 0.05.
effect on malarial infection in an endemic area such as Nyando. However, our unadjusted results showed an inverse association between homozygous \( \alpha^+ \)-thalassemia and low RBP, this relationship was no longer significant after we controlled for other variables. However, our fully adjusted results were close to statistical significance, and our nonsignificant finding may be a result of the low number of children in our study population who had homozygous \( \alpha^+ \)-thalassemia. If homozygosity for \( \alpha^+ \)-thalassemia and RBP levels is truly associated, studies of potential mechanisms behind this association and studies of the relationship between \( \alpha^+ \)-thalassemia and VAD in a population with a lower prevalence of inflammation may be warranted.

Our finding that HbAS was not associated with stunting or anemia was inconsistent with previous findings. However, there is evidence that biological interactions among co-inherited hemoglobinopathies may have limited our ability to detect any such reduction in prevalence associated with HbAS. Additionally, because of low sample sizes, we were unable to assess nutritional status with HbSS, which has been shown to be associated with stunting and micronutrient deficiencies.

Our findings also did not indicate a relationship between nutritional outcomes and either G6PD deficiency or Hp polymorphism, which was unexpected given that both blood disorders have previously been associated with malaria. Theoretically, people at increased malarial risk from co-inherited hemoglobinopathies may have limited exposure to hemolytic events from G6PD deficiency would be at higher risk for chronic anemia, with expected consequences on growth indicators.

It is important to note that in low-resource environments where the prevalence of disease is high throughout the population, any additional disease attributable to inherited blood disorders may be difficult to detect. In addition, as a cross-sectional study, survival bias is a potential confounding factor in the relationship between disease prevalence and either HbSS or G6PD deficiency. In our study cohort, HbSS children were, on average, 8 months younger than those with other genotypes, suggesting that older HbSS children may not have survived. Severe symptoms of G6PD deficiency include neonatal complications such as jaundice, which may lead to death if not treated. As such, we were not able to assess the relationship between nutrition and blood disorders among children with severe forms of these diseases.

In communities with a higher SES distribution and lower rates of child morbidity and mortality attributable to poor sanitation and infectious diseases, child survival will likely be more common. As health outcomes improve in populations with a high prevalence of inherited blood disorders and more children reach adulthood, it will be even more important to understand how inherited blood disorders may be associated with poor nutrition.

**Study strengths and limitations.** A strength of this study was our analysis of data based on the measurement of multiple nutrition biomarkers and the genotyping of multiple blood disorders. However, because of the cross-sectional survey design, any associations between blood disorders and conditions related to malnutrition do not necessarily indicate a causal relationship. In addition, the use of OR in a cross-sectional study overstates the prevalence ratio because the outcomes studied in this analysis are common.

Other study limitations included potential information bias from self-reported household data, analysis of data from a relatively small area of Kenya (Nyando Division), which may not be representative of the country as a whole, and inability to assess to what magnitude blood disorders change hemologic nutrition indicators. In addition, the survey tool did not collect data on other potential confounding factors such as helminth or roundworm parasite infections, vitamin A supplementation, and recent treatment with antimalarial medication, which limited analyses.

**CONCLUSION**

Our findings showed that in western Kenya, an area with a high prevalence of childhood malnutrition, inherited blood disorders are not associated with most indicators of poor nutritional status. There may be limited value in assessing blood disorders for measuring certain nutritional outcomes, such as growth. The only significant association we found was between \( \alpha^+ \)-thalassemia and anemia. Regional anemia prevalence estimates should take this association into consideration when interpreting anemia etiologies and when recommending nutritional interventions such as iron supplementation.

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**Authors’ addresses:** Becky L. Tsang, Prevention Research Branch, Centers for Disease Control and Prevention, Atlanta, GA, E-mail: woh3@cdc.gov. Kevin M. Sullivan, Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, E-mail: edckms@sphealth.emory.edu. Laird J. Ruth and Parminder S. Suchdev, Nutrition Branch, Centers for Disease Control and Prevention, Atlanta, GA, E-mails: lruth@cdc.gov and dvo8@cdc.gov. Thomas N. Williams, Centre for Geographic Medicine Research-Coast, Kenya Medical Research Institute, Kilifi, Kenya, E-mail: twilliams@kilifi.kemri-wellcome.org.

**REFERENCES**


