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# Age, Ethnicity, Glucose-6-Phosphate Dehydrogenase Deficiency, Micronutrient Powder Intake, and Biomarkers of Micronutrient Status, Infection, and Inflammation Are Associated with Anemia Among Children 6–59 Months in Nepal

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## Abstract

**Background—**Anemia is a major concern for children in Nepal; however, little is known about context-specific causes of anemia.

**Objective—**We used cross-sectional data from the 2016 Nepal National Micronutrient Status Survey to evaluate factors associated with anemia in a nationally representative, population-based sample of children 6–59 mo ($n$ = 1367).

**Methods—**Hemoglobin, biomarkers of iron status and other micronutrients, infection, inflammation, and blood disorders were assessed from venous blood samples. Soil-transmitted helminth (STH) and *Helicobacter pylori* infections were assessed from stool. Anthropometry was measured with standard procedures. Sociodemographic and household characteristics, diet, micronutrient powder (MNP) intake, pica, and morbidity recall were ascertained by caregiver interview. Multivariable logistic regression that accounted for complex sampling design, determined predictors of anemia (hemoglobin <11.0 g/dL, altitude adjusted); candidate predictors were variables with $P < 0.05$ in bivariate models.

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Supplemental Tables 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn.

**Results—**Anemia prevalence was 18.6% (95% CI: 15.8, 21.4). MNP intake [adjusted OR (AOR): 0.25, 95% CI: 0.07, 0.86], log (ln) ferritin (μg/L) (AOR: 0.49, 95% CI: 0.38, 0.64), and ln RBP (μmol/L) (AOR: 0.42, 95% CI: 0.18, 0.95) were associated with reduced odds of anemia. Younger age (6–23 mo compared with 24–59 mo; AOR: 2.29, 95% CI: 1.52, 3.46), other Terai ethnicities (AOR: 2.59, 95% CI: 1.25, 5.35) and Muslim ethnicities (AOR: 3.15, 95% CI: 1.30, 7.65) relative to Brahmin/Chhetri ethnicities, recent fever (AOR: 1.68, 95% CI: 1.08, 2.59), ln C-reactive protein (mg/L) (AOR: 1.23, 95% CI: 1.03, 1.45), and glucose-6-phosphate dehydrogenase deficiency (AOR: 2.84, 95% CI: 1.88, 4.30) were associated with increased odds of anemia.

**Conclusion—**Both nonmodifiable and potentially modifiable factors were associated with anemia. Thus some but not all anemia might be addressed through effective public health policy, programs, and delivery of nutrition and infection prevention and control. *J Nutr* 2019;00:1–9.

### Keywords

anemia; micronutrient status; child nutrition; Nepal; iron deficiency; vitamin A deficiency; infection

## Introduction

Worldwide, anemia affects an estimated 43% of children aged <5 y (1) and is thought to contribute to an estimated 591,000 perinatal deaths annually (2). Globally, iron deficiency is estimated to cause half of anemias; however, the proportion likely varies by population (2). Beyond iron deficiency, numerous other factors contribute to anemia including problems producing hemoglobin (inflammation-induced iron sequestration, thalassemias), lack of sufficient DNA precursors (folate and vitamin B-12 deficiencies), erythrocyte damage and hemolysis [parasitic infections, blood disorders such as glucose-6-phosphate dehydrogenase deficiency (G6PD), immune-mediated destruction], and blood loss (Figure 1).

Historically, Nepal has had a high anemia burden—with prevalence levels of severe public health significance, according to WHO classifications (3). In 2002, the government of Nepal developed a National Strategy for the Control of Anemia among Women and Children. National-level initiatives targeting anemia among children include interventions to improve infant and young child feeding (IYCF) practices for children aged <2 y. Other related programs include biannual vitamin A supplementation and deworming during child health day campaigns. Despite these initiatives, the prevalence of anemia among children 6–59 mo increased from 46% in 2011 to 53% in 2016, according to Demographic and Health Surveys (DHS) (4).

Understanding the context-specific drivers of anemia is crucial to developing effective, evidence-based public health programming. Although the physiology of anemia is relatively well understood globally, less is known about context-specific determinants of anemia among children in Nepal. Previous studies in Nepal have focused on iron status, body size, infant feeding practices, maternal health status, and sociodemographic characteristics (5, 6). Because collecting biological data on other known contributors to anemia can be logistically difficult and expensive, these indicators are not usually included in large-scale population-based surveys. To address this important knowledge gap in context-specific drivers of

anemia, the Nepal National Micronutrient Status Survey (NNMSS) collected data on micronutrient status and potential causes of anemia with the goal of identifying the etiology of anemia and guiding programmatic decision-making. Although the data presented in this paper are comprehensive, it is not sufficient to identify population attributable fractions of anemia; however, the information can be used to help prioritize anemia interventions. These analyses evaluated the factors associated with anemia among children 6–59 mo in Nepal.

## Methods

### Study population

The 2016 NNMSS was implemented by New ERA with support from the Nepal Ministry of Health and Population (MoHP), EU, USAID, UNICEF Nepal, and the US Centers for Disease Control and Prevention. Through use of stratified multistage cluster sampling without replacement, we selected 180 clusters from 15 strata with probability proportional to size. We then selected 24 households in each cluster by systematic sampling ($n = 4320$). After enumerating all children 6–59 mo (henceforth referred to as children), we sampled at random 12 children from selected households from each cluster. The survey aimed to collect data from 2160 children; sample size was calculated assuming 46% anemia prevalence based on the 2011 DHS, ±3.5% precision nationally, a design effect of 2.25, and household and individual response rates of 95% and 90%, respectively (7). Full details about the study area, study population, and sampling strategy are available in the NMSS Report (8).

Of the 2160 children planned for data collection, 1728 children were available in the selected clusters. Of those, 1709 (98.9%) completed the interview ($n = 5$ refusals and $n = 14$ were unreachable). We excluded participants with missing or invalid values for hemoglobin ($n = 77$), other blood-based indictors ($n = 75$), stool-based indicators ($n = 158$), anthropometry ($n = 18$), and questionnaire data ($n = 33$) for a final analytic sample of 1367 children (79.1% of available children). With the exception of age, ecological zone, and ethnicity, children who were excluded did not differ with respect to anemia status or other major sociodemographic characteristics from those included in the analytic sample (Supplemental Table 1).

Ethical approval for the study was granted by the Nepal Health Research Council. The respondent for the household interview signed informed consent, and the legal guardians or parents signed informed consent on behalf of their children.

### Data collection

**Anthropometry—**Recumbent length (6–23 mo) or standing height (24–59 mo) was measured without shoes to the nearest 0.1 cm with a Shorr-Board. Weight was measured with light clothing to the nearest 100 g with an electronic SECA digital scale.

**Biological specimens—**Blood and stool samples were collected to assess blood disorders and micronutrient, infection, and inflammation status. Trained phlebotomists collected nonfasted venous blood samples at the time of interview following standard procedures. Each child's caregiver received a stool collection kit and instructions on the

collection, transfer, and storage of the stool. The study team retrieved stool cups from households within 24 h and stored samples in a cold box.

Laboratory technicians and pathologists processed and read the specimens at a lab station in each cluster. Hemoglobin (HemoCue® Hb 301 analyzer), malaria (CareStart™ malaria antigen combo rapid test kit for *P. falciparum* and *P. vivax*), and visceral leishmaniasis (IT LEISH rK39 antigen rapid test kit) were analyzed at the households. Stool samples were examined for soil-transmitted helminths (STH) (hookworm, *Ascaris*, and *Trichuris*) by microscopic examination within 24 h of collection with the Kato Katz method (9). For blood disorders, whole blood samples were transported to the pathology laboratory in Kathmandu within 7 d of sample collection, maintaining cold chain. Plasma, serum, and stool samples were transported to the National Public Health Laboratory and stored in −86°C freezers until analysis.

VitMin Lab (Willstaett, Germany) analyzed serum C-reactive protein (CRP), α−1-acid glycoprotein (AGP), ferritin, transferrin receptor (sTfR), and retinol-binding protein (RBP) with a sandwich ELISA (10). RBC folate was analyzed with a microbiological assay (11). Serum zinc was analyzed with atomic absorption spectrometry. For blood disorders, G6PD was assessed by the Access Bio Korea Inc.CareStart ™ G6PD Biosensor, $\alpha$- and $\beta$-thalassemia and sickle cell by PCR, hemoglobin E by DNA, and complete blood count by HPLC. *Helicobacter pylori* was assessed in stool with an immunoassay (EDI TM Fecal *H. pylori* antigen ELISA kit).

**Sociodemographic, health, and other questionnaire data—**Sociodemographic characteristics; bed net use; morbidity recall; housing, water, and sanitation characteristics; treatment for acute malnutrition; previous-day recall of breastfeeding and of specific liquids and foods consumed (12), fortified infant foods, tea, and foods prepared with purchased fortifiable staple foods; micronutrient supplement intake; pica; and receipt of high-dose vitamin A supplementation and deworming tablets were collected from caregivers by an in-person interview-administered questionnaire. Household food security was ascertained with a 9-item questionnaire about access to adequate and preferred foods (13).

## Variable specification

**Anemia—**Hemoglobin was adjusted for altitude with standard procedures (3).We defined anemia as altitude-adjusted hemoglobin <11.0 g/dL (3). Anemia severity was classified as mild (altitude-adjusted hemoglobin 10.0–10.9 g/dL), moderate (altitude-adjusted hemoglobin 7.0–9.9 g/dL), and severe (altitude-adjusted hemoglobin <7.0 g/dL) (3).

**Anthropometry—**We calculated length/height-for-age (HAZ), weight-for-age (WAZ), and weight-for-length/height (WHZ) *z* scores for children with use of the WHO child growth standards (14). Stunting, underweight, and wasting were classified as HAZ, WAZ, and WHZ <−2 SD, respectively (14).

**Biomarkers of nutrition status—**To adjust for inflammation, we regression-adjusted ferritin, sTfR, RBP, and zinc to a pooled country reference with CRP and AGP (ferritin, RBP, zinc) or AGP only (sTfR) (15). We defined iron deficiency as adjusted ferritin <12.0

μg/L (3) and iron deficiency anemia as altitude-adjusted hemoglobin <11.0 g/dL and adjusted ferritin <12.0 μg/L. Vitamin A deficiency was defined as adjusted RBP <0.69 μmol/L. To find the population-specific RBP cutoff, we regressed RBP on retinol to determine the RBP equivalent of retinol <0.70 μmol/L based on the subsample of 200 children for whom serum retinol was assessed with HPLC from the same blood draw as RBP (16). We classified risk of folate deficiency as RBC folate <305.0 nmol/L (17). Zinc deficiency was classified as adjusted zinc <65.0 μg/dL for nonfasted, morning samples and <57.0 μg/dL for nonfasted afternoon samples (18).

**Infection, inflammation, and blood disorders—**We defined STH infection as presence of any eggs in stools compared with no eggs. Malaria, *H. pylori*, visceral leishmaniosis, and fever, diarrhea, and cough during the 2 wk preceding the survey were included as binary variables (yes/no). We included CRP and AGP as continuous variables. Blood disorders were categorized as: *1*) G6PD; and *2*) hemoglobinopathies.

**Dietary intake—**Consumption of flesh, organ, or blood-based foods, legumes, green leafy vegetables, vitamin A-rich fruits and vegetables, fortified infant foods (e.g., cerelac, nutrimix, and other fortified complementary foods), and tea during the day preceding the survey were included as binary variables (yes/no).We defined minimum dietary diversity as intake from ≥4 of the 7 main food groups the day preceding the survey (12). Consumption of foods prepared with purchased fortifiable wheat flour and foods prepared with purchased fortifiable vegetable ghee during the week preceding the survey were included as binary variables (yes/no). We defined pica as any consumption of clay, earth, termite mounds, ice, uncooked rice, or starch during the week preceding the survey.

**Child health—**Intake of micronutrient powder (MNP), iron syrup or tablets, and zinc supplements during the week preceding the survey were included as binary variables (yes/no). We included treatment for marasmus or kwashiorkor during the 12 mo preceding the survey, receipt of vitamin A supplementation, and receipt of deworming tablets during the previous child health campaign as binary variables (yes/no). Bed net use was categorized as always use bed net compared with sometimes or never use bed net.

**Sociodemographic variables—**We categorized age as 6–23 mo and 24–59 mo. Ethnicity was categorized as Brahmin/Chettri, Dalit, Janajati, other Terai ethnicities (including Terai/Madhesi ethnicities but not including Terai or Madhesi Brahmin or Chettri), Newar, and Muslim (19). We defined improved water source as having piped water, tube well borehole, protected well or spring, stone tap, rainwater, or bottled water (20). Severe household food insecurity was defined as households who often cut back on meal size or number of meals and/or ever experienced any of the 3most severe conditions (no food to eat of any kind in the household because of lack of resources to get food; any household member goes to sleep at night hungry because there was not enough food; and any household member goes a whole day and night without eating anything because there was not enough food) during the 12 mo preceding the survey (13). We included improved water source, open defecation, earth floor, and severe household insecurity as binary variables (yes/no). Household location was defined as rural compared with urban per Nepal

administrative classifications. We created a household wealth score through use of principal components analysis of housing characteristics and assets, then divided wealth into tertiles.

### Statistical methods

We set micronutrient status indicators to missing where outliers were likely because of processing error or sample contamination ($n$ = 3 for zinc, $n$ = 6 for RBC folate, $n$ = 4 for RBP, $n$ = 14 for sTfR, and $n$ = 5 for ferritin). Biologically implausible WAZ (<−6 or >5),HAZ (<−6 or >6), and WHZ <−5 or >5) were set to missing based on WHO child growth guidelines ($n$ = 1 for WAZ, $n$ = 11 for HAZ, and $n$ = 13 for WHZ) (14).

We assessed for influential outliers with Cook's D Method and Studentized Pearson Residuals (21). Three outliers were detected for ferritin (84 μg/L, 119.4 μg/L, and 125.8 μg/L); however, these values are biologically plausible, so we retained them in the analysis. We assessed nonlinearity between continuous predictor variables and log-odds of anemia with the Box-Tidwell test (22). Because CRP, ferritin, and RBP were nonlinear, we log transformed these variables.

To identify factors that were associated with anemia in our study population, we conducted bivariate analyses between anemia status and the candidate predictors with use of Rao-Scott chi-square tests and linear contrast tests for categorical and continuous predictor variables, respectively. A data manifest is presented in Supplemental Table 2. Categorical predictor variables with more than 2 levels (e.g., ethnicity) were tested as a group and not each level individually. In the multivariable logistic regression model, we included all candidate predictors with $P < 0.05$ in bivariate models. Eigenvalues <0.01 and conditionality index >30 identified potential collinearity. We assessed the model's goodness of fit with Harrell's C statistic (23).

All analyses were conducted in SAS v.9.4 (SAS Institute Inc.) with PROC SURVEY procedures. We accounted for complex sample design with sampling weights and SAS STRATA and CLUSTER statements. In addition, we accounted for clustering at the household level; 1033 households had 1 sampled child while 149 households had 2 sampled children, and 12 households had 3 sampled children. Statistical significance was set a priori at 2-sided $P < 0.05$.

## Results

Overall, 18.6% (95% CI: 15.8, 21.4) of children 6–59 mo had anemia (Table 1), of which 74.4% (95% CI: 67.7, 81.1) cases were mild and 25.5% (95% CI: 18.8, 32.1) of cases were moderate.

Candidate predictors ($P < 0.05$ in bivariate analyses) in the multivariable model included both nonmodifiable (age, ecological zone, ethnicity, household wealth, G6PD) and potentially modifiable factors [open defecation, stunting, underweight, fever, diarrhea, inflammation (CRP, AGP), micronutrient status (ferritin, sTfR, RBP), MNP intake, bed net use, and deworming]. We removed sTfR from the model because of collinearity with ferritin.

Ferritin is the WHO-recommended indicator to assess iron status (3). Harrell's C statistic of 0.77 suggests that our multivariable model had good fit (23).

In the multivariable model, children with recent fever had higher odds of anemia [adjusted OR (AOR): 1.68, 95% CI: 1.08, 2.59] (Table 2). Log (ln) CRP (mg/L) was associated with increased odds of anemia (AOR: 1.23, 95% CI: 1.03, 1.45).

Child micronutrient status was also associated with anemia. Ln ferritin (μg/L) and ln RBP (μmol/L) were both associated with reduced odds of anemia (AOR: 0.49, 95% CI: 0.38, 0.64 and AOR: 0.42, 95% CI: 0.18, 0.95, respectively). Although overall MNP intake the week preceding the survey was low (1.9%,95% CI: 0.9, 2.8), MNP was associated with 75% lower odds of anemia (AOR: 0.25, 95% CI: 0.07, 0.86).

Three nonmodifiable indicators were also associated with anemia. Children 6–23 mo had 2.29 times higher odds of anemia compared to children 24–59 mo (AOR: 2.29, 95% CI: 1.52, 3.46). Relative to Brahmin/Chettri ethnicities, Other Terai ethnicities and Muslim ethnicities had 2.59 (95% CI: 1.25, 5.35) and 3.15 (95% CI: 1.30, 7.65) times higher odds of anemia, respectively. G6PD was associated with a nearly 3-fold increase in anemia odds relative to those without this enzyme deficiency (AOR: 2.84, 95% CI: 1.88, 4.30).

## Discussion

Through use of a national representative sample of children 6–59 mo, we identified both potentially modifiable and nonmodifiable factors associated with anemia in Nepal. In total, 18.6% of children had anemia—a prevalence level of mild public health significance, according to the WHO (3). Potential modifiable factors including fever and acute inflammation (CRP) were associated with increased odds of anemia while MNP intake, ferritin, and RBP were associated with reduced odds of anemia. Nonmodifiable factors included age, ethnicity, and presence of G6PD. Overall, this analysis and the broader literature suggest strengthening nutrition and infection prevention and control strategies in Nepal may address some, but not all, anemia among children 6–59 mo.

Both iron (ferritin) and vitamin A (RBP) were inversely associated with anemia odds. Among those with anemia, 54.2% (95% CI: 46.2, 62.1) had iron deficiency and 5.0% (95% CI: 1.7, 8.3) had vitamin A deficiency. Iron deficiency is considered the leading nutritional cause of anemia globally (2), and vitamin A is essential for erythropoiesis, mobilization of iron stores, and immune function (24). We found no differences in consumption of iron-rich or vitamin A-rich foods, fortified infant foods, foods prepared with purchased wheat flour (potentially fortified with iron and vitamin A), or minimum dietary diversity by anemia status. Our findings are similar to those from a study of children aged 4–17 mo in south central Nepal that found no associations between dietary intake indicators and anemia (5). Although we were unable to estimate total intake of either iron or vitamin A, consumption of nutrient-dense food groups was low in the overall population.

MNP intake during the week before the survey was associated with 75% lower odds of anemia. MNP are single-serve sachets of iron, vitamin A, and other micronutrients used to fortify foods right before consumption to reduce anemia and iron deficiency (25). For

children aged 2–12 y, a 2016 systematic review which included studies from countries such as India, Bangladesh, and Kenya found that iron-containing MNP reduced anemia prevalence by 34% (prevalence ratio: 0.66; 95% CI: 0.49, 0.88) and the prevalence of iron deficiency by 65% (prevalence ratio: 0.35, 95% CI: 0.27, 0.47) relative to a placebo (26). Because the MNP formulation in Nepal includes 15 micronutrients, it could be addressing deficiencies for which we lack data, such as riboflavin and thiamin.

National IYCF programs focused on supporting intake of iron- and vitamin A-rich food sources, as well as effective implementation and sustained rollout of the MNP intervention may help reduce anemia by improving overall micronutrient status. IYCF programs are the primary mechanism to address nutritional status among children 6–59 mo in Nepal. The MoHP's strategies include supporting optimal breastfeeding and promoting complementary feeding practices by promoting diverse diet of nutrient-rich, energy-dense foods with specific emphasis on the intake of iron- and vitamin A-rich foods starting at age 6 mo. By adhering to the advice in the program, improving diets should improve both iron and vitamin A status among children. In addition, the MoHP has integrated MNP distribution into the IYCF program for children 6–23 mo in 23 of the country's 77 districts. Expanding MNP distribution nationwide and potentially expanding the target age range to 6–59 mo should improve iron and vitamin A status and reduce anemia.

Acute inflammation and fever were associated with increased odds of anemia. Inflammation can cause anemia through immune-mediated mechanisms wherein cytokines cause dysregulation of iron homeostasis (27). Exposure to infection—especially during periods of rapid growth—increases risk of iron deficiency and anemia (28). Given the high prevalence of infection and inflammation and their role in mucosal absorption of iron (29), both low intake and poor absorption may influence iron deficiency and anemia in the survey population.

We found several nonmodifiable factors associated with anemia. Consistent with studies in Nepal and elsewhere, younger age was associated with higher odds of anemia among children (5, 30–32). The association between age and anemia could be a result of changes in diet in the postweaning period; however, we were unable to explore these potential relationships because of limited dietary data among children 24–59 mo. We also found that, relative to Brahmin/Chhetri ethnicities, other Terai ethnicities and Muslim ethnicities had significantly increased odds for anemia. Ethnicity was also a significant determinant of anemia among 4–17 mo children in south central Nepal (5). While age and ethnicity are nonmodifiable, information about anemia patterning could be used to target anemia prevention and control initiatives.

Children with G6PD had nearly 3 times higher odds of anemia in our analyses. Although many individuals with G6PD are asymptomatic, infection, illness, and exposure to certain foods and drugs including sulfonamides, some anthelmintics, and quinine-derived antimalarials can induce acute hemolysis (33). Although inherited disorders are nonmodifiable, acute hemolytic anemia could be prevented by identifying cases with newborn screening, informing those affected of their risk and providing them information about which foods and drugs to avoid (34). Further, understanding patterning of G6PD is

useful for program planning and crucial to make sense of monitoring and evaluation data. Even with well-designed and implemented anemia control programs, G6PD prevalence might explain differential success in reducing anemia.

Our findings suggest a significantly lower anemia prevalence compared to the 2016 DHS, which reported 53% prevalence among children 6–59 mo (4). In a comparison of DHS and national micronutrient surveys conducted simultaneously within the same country, DHS reported lower hemoglobin concentrations and larger standard errors among children 6–59 mo relative to national micronutrient surveys, resulting in 20–35 percentage point differences in anemia prevalence (35). Differences in hemoglobin measurement possibly account for some of the difference in anemia prevalence. DHS used single drops of blood from capillary blood samples collected by wicking method and measured on a HemoCue® Hb 201 analyzer while the NNMSS used venous blood samples and measured on a HemoCue® Hb 301 analyzer. To date, several studies have explored the variation in hemoglobin concentrations by blood type and instrument; however, available data does not allow the distinction of venous compared with capillary blood from instrument/assessment method variation (36). Although further analysis is needed to better understand the differences in anemia prevalence in Nepal, the discrepancies between surveys conducted close in time in Nepal are not unique.

We used comprehensive, nationally representative data on multiple potential causes of anemia—many of which are rarely included in large-scale surveys in low- and middle-income countries. To our knowledge, this analysis is the first to examine a wide range of known potential causes of anemia in a nationally representative sample of children 6–59 mo in Nepal. The NNMSS did not collect data on all micronutrients for which deficiency could lead to anemia. Although we measured plasma vitamin B-12, they were excluded from these analyses because of issues with data quality. We were unable to assess the role of some key IYCF indicators because these questions were only asked of children 6–23 mo. Dietary recall questions were limited in scope. Caregiver recall could have introduced bias for report of IYCF and consumption data, vitamin and mineral supplement intake, treatment for malnutrition, and household food insecurity; however, potential bias was not likely to be differential by anemia status because caregivers completed the survey questionnaire before the hemoglobin assessment. *P* values were not adjusted for multiple testing, which may have introduced the potential for type I error. Reduced sample size because of missing data may have reduced our power to detect small effect sizes. Because we used cross-sectional data, we were unable to determine causality between the candidate predictors and anemia status or assess population attributable fraction.

Our analysis suggests a combination of prevention and treatment strategies effectively implemented could potentially reduce anemia among children 6–59 mo in Nepal, including addressing micronutrient status and infections. Finally, while nonmodifiable, understanding the patterning of blood disorders among children in Nepal can help inform program planning and provide context to program monitoring and evaluation data.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations used

| | |
|---|---|
| **AGP** | α-1-acid glycoprotein |
| **AOR** | adjusted OR |
| **CRP** | C-reactive protein |
| **DHS** | Demographic and Health Surveys |
| **G6PD** | glucose-6-phosphate dehydrogenase deficiency |
| **HAZ** | length/height-for-age *z* score |
| **IYCF** | infant and young child feeding |
| **MNP** | micronutrient powder |
| **MoHP** | Ministry of Health and Population |
| **NNMSS** | Nepal National Micronutrient Status Survey |
| **RBP** | retinol-binding protein |
| **STH** | soil-transmitted helminths |
| **sTfR** | transferrin receptor |
| **WAZ** | weight-for-age *z* score |
| **WHZ** | weight-for-length/height *z* score |

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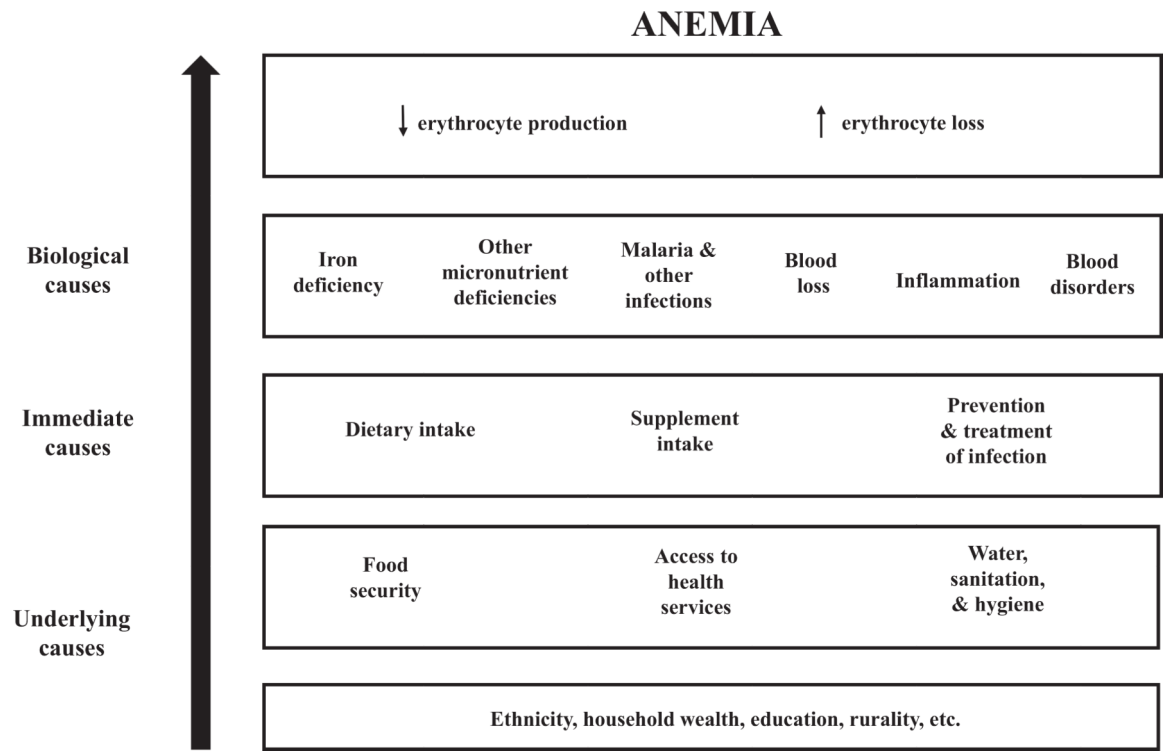


**FIGURE 1.**

Globally, iron deficiency is estimated to cause half of anemias; however, the proportion likely varies by population. Beyond iron, additional factors contribute to anemia through underproduction or excessive loss of RBCs including problems producing hemoglobin (inflammation-induced iron sequestration, thalassemias), lack of sufficient DNA precursors (folate and vitamin B-12 deficiencies), erythrocyte damage and hemolysis (parasitic infections, blood disorders like glucose-6-phosphate dehydrogenase deficiency (G6PD), immune-mediated destruction), and blood loss. Further, food security, access to health services, and sociodemographic characteristics underlie many of the intermediate causes of anemia, such as dietary intake.

**TABLE 1**

Selected sociodemographic and health characteristics of children 6–59 mo, by anemia status, Nepal National Micronutrient Status Survey, Nepal, 2016 ($n$ = 1367)[1]

| | Anemia[2] [$n$ = 231, 18.6% (95% CI: 15.8, 21.4)] | | No anemia[2] [$n$ = 1136, 81.4% (95% CI: 78.6, 84.2)] | | | Total ($n$ = 1367) | |
|---|---|---|---|---|---|---|---|
| | $n$ | | $n$ | | $P$[3] | $n$ | |
| Sociodemographic characteristics | | | | | | | |
| Sex, % | | | | | 0.4 | | |
| Female | 129 | 57.7 (49.9, 65.5) | 575 | 54.1 (50.8, 57.4) | | 704 | 54.8 (51.7, 57.8) |
| Male | 102 | 42.3 (34.5, 50.1) | 561 | 45.9 (42.6, 49.2) | | 663 | 45.2 (42.2, 48.3) |
| Age group, % | | | | | <0.0001 | | |
| 6–23 mo | 113 | 47.9 (40.7, 55.1) | 265 | 24.2 (21.3, 27.1) | | 378 | 28.6 (25.8, 31.4) |
| 24–59 mo | 118 | 52.1 (44.9, 59.3) | 871 | 75.8 (72.9, 78.7) | | 989 | 71.4 (68.6, 74.2) |
| Location, % | | | | | 0.4 | | |
| Rural | 204 | 85.6 (78.7, 92.6) | 989 | 88.3 (86.1, 90.5) | | 1193 | 87.8 (85.5, 90.1) |
| Urban | 27 | 14.4 (7.4, 21.3) | 147 | 11.7 (9.5, 13.9) | | 174 | 12.2 (9.9, 14.5) |
| Ecological zone, % | | | | | 0.0007 | | |
| Mountain | 34 | 6.6 (4.2, 8.9) | 194 | 8.4 (7.5, 9.3) | | 228 | 8.1 (7.4, 8.8) |
| Hill | 83 | 33.8 (26.4, 41.2) | 511 | 46.6 (44.1, 49.1) | | 594 | 44.2 (42.1, 46.3) |
| Terai | 114 | 59.6 (52.0, 67.3) | 431 | 45.0 (42.4, 47.5) | | 545 | 47.7 (45.5, 49.9) |
| Household wealth tertile | | | | | 0.03 | | |
| Poorest | 88 | 26.5 (19.9, 33.1) | 418 | 29.3 (26.2, 32.4) | | 506 | 28.8 (26.0, 31.6) |
| Middle | 85 | 43.5 (34.5, 52.4) | 351 | 32.1 (28.5, 35.8) | | 436 | 34.2 (30.7, 37.8) |
| Wealthiest | 58 | 30.0 (21.8, 38.3) | 367 | 38.6 (34.9, 42.4) | | 425 | 37.0 (33.5, 40.5) |
| Ethnicity, % | | | | | <0.0001 | | |
| Brahmin/Chettri | 67 | 22.4 (16.1, 28.7) | 421 | 33.6 (30.1, 37.1) | | 488 | 31.5 (28.4, 34.6) |
| Dalit | 51 | 16.6 (10.1, 23.0) | 246 | 19.0 (16.1, 21.9) | | 297 | 18.5 (15.9, 21.2) |
| Janajati | 64 | 26.2 (18.9, 33.4) | 339 | 29.7 (26.2, 33.2) | | 403 | 29.0 (25.9, 32.2) |
| Other Terai ethnicities[4] | 29 | 23.9 (15.9, 32.0) | 61 | 10.4 (7.6, 13.1) | | 90 | 12.9 (10.1, 15.7) |
| Newar | 5 | 1.9 (0.0, 3.8)[5] | 39 | 4.3 (2.7, 6.0) | | 44 | 3.9 (2.5, 5.3) |

| | Anemia[2] [*n* = 231, 18.6% (95% CI: 15.8, 21.4)] | | No anemia[2] [*n* = 1136, 81.4% (95% CI: 78.6, 84.2)] | | | Total (*n* = 1367) | |
|---|---|---|---|---|---|---|---|
| | *n* | | *n* | | *P*[3] | *n* | |
| Muslim | 15 | 9.1 (3.0, 15.1) | 30 | 3.0 (1.9, 4.2) | | 45 | 4.2 (2.6, 5.7) |
| Improved water source,[6] % | 224 | 96.8 (93.8, 99.7) | 1095 | 96.1 (94.6, 97.6) | 0.7 | 1319 | 96.2 (94.8, 97.6) |
| Open defecation, % | 34 | 24.7 (16.5, 32.9) | 121 | 16.2 (13.0, 19.4) | 0.03 | 155 | 17.8 (14.7, 20.9) |
| Earth floor, % | 175 | 70.5 (62.2, 78.7) | 779 | 65.1 (61.4, 68.8) | 0.2 | 954 | 66.1 (62.6, 69.6) |
| Severe household food insecurity, % | 19 | 6.4 (2.9, 9.9) | 90 | 6.6 (4.9, 8.3) | 0.9 | 109 | 6.6 (5.0, 8.1) |
| Health characteristics | | | | | | | |
| Hemoglobin,[7] g/dL | 231 | 10.2 (10.0, 10.3) | 1136 | 12.2 (12.2, 12.3) | | 1367 | 11.8 (11.7, 11.9) |
| Anemia severity,[8] % | | | | | | | |
| No anemia | 0 | 0.0 (0.0, 0.0) | 1136 | 100.0 (100.0, 100.0) | | 1136 | 81.4 (78.6, 84.2) |
| Mild | 170 | 74.4 (67.7, 81.1) | 0 | 0.0 (0.0, 0.0) | | 170 | 13.8 (11.4, 16.3) |
| Moderate | 60 | 25.5 (18.8, 32.1) | 0 | 0.0 (0.0, 0.0) | | 60 | 4.7 (3.3, 6.2) |
| Severe | 1 | 0.2 (0.0, 0.5)[5] | 0 | 0.0 (0.0, 0.0) | | 1 | 0.0 (0.0, 0.1)[5] |
| Anthropometry,[9] % | | | | | | | |
| Stunting | 105 | 43.7 (36.1, 51.4) | 408 | 33.1 (29.9, 36.3) | 0.01 | 513 | 35.1 (32.1, 38.1) |
| Underweight | 90 | 39.0 (31.7, 46.4) | 322 | 28.2 (24.9, 31.5) | 0.006 | 412 | 30.2 (27.2, 33.2) |
| Wasting | 29 | 13.5 (8.3, 18.7) | 117 | 11.7 (9.2, 14.2) | 0.5 | 146 | 12.0 (9.8, 14.3) |
| Treatment for marasmus/kwashiorkor,[10] % | 3 | 0.5 (0.0, 1.0)[5] | 13 | 1.1 (0.3, 2.0) | 0.2 | 16 | 1.0 (0.3, 1.7) |
| 2-wk morbidity recall, % | | | | | | | |
| Fever | 102 | 45.8 (37.4, 54.3) | 396 | 34.2 (30.9, 37.6) | 0.009 | 498 | 36.4 (33.1, 39.6) |
| Diarrhea | 57 | 30.1 (22.1, 38.1) | 205 | 17.8 (15.2, 20.5) | 0.001 | 262 | 20.1 (17.4, 22.8) |
| Cough | 83 | 38.8 (30.5, 47.2) | 428 | 38.0 (34.5, 41.5) | 0.8 | 511 | 38.1 (34.9, 41.4) |
| CRP, mg/L | 231 | 0.88 (0.64, 1.19) | 1136 | 0.47 (0.42, 0.52) | <0.0001 | 1367 | 0.52 (0.47, 0.58) |
| AGP, g/L | 231 | 0.85 (0.78, 0.93) | 1136 | 0.73 (0.71, 0.76) | 0.0009 | 1367 | 0.75 (0.73, 0.78) |
| Malaria, % | 0 | 0.0 (0.0, 0.0) | 0 | 0.0 (0.0, 0.0) | — | 0 | 0.0 (0.0, 0.0) |
| *Helicobacter pylori*, % | 32 | 16.2 (9.9, 22.5) | 240 | 20.3 (17.4, 23.1) | 0.3 | 272 | 19.5 (16.9, 22.1) |
| Visceral leishmaniasis, % | 0 | 0.0 (0.0, 0.0) | 3 | 0.2 (0.0, 0.4) [5] | — | 3 | 0.1 (0.0, 0.3) [5] |
| Soil-transmitted helminth infection,[11] % | 34 | 17.3 (10.6, 23.9) | 138 | 11.5 (9.3, 13.7) | 0.07 | 172 | 12.6 (10.4, 14.8) |

| | Anemia[2] [*n* = 231, 18.6% (95% CI: 15.8, 21.4)] | | No anemia[2] [*n* = 1136, 81.4% (95% CI: 78.6, 84.2)] | | | Total (*n* = 1367) | |
|---|---|---|---|---|---|---|---|
| | *n* | | *n* | | *P*[3] | *n* | |
| G6PD, % | 68 | 33.2 (25.8, 40.6) | 148 | 12.8 (10.5, 15.1) | <0.0001 | 216 | 16.6 (14.2, 19.0) |
| Hemoglobinopathies,[12] % | 27 | 12.7 (7.5, 17.9) | 75 | 8.1 (6.1, 10.2) | 0.06 | 102 | 9.0 (7.0, 10.9) |
| Caregiver report of Child Health Day participation, % | | | | | | | |
| Vitamin A supplementation | 213 | 92.1 (87.9, 96.2) | 1062 | 93.2 (91.3, 95.0) | 0.6 | 1275 | 92.9 (91.2, 94.7) |
| Deworming | 170 | 74.9 (68.3, 81.5) | 970 | 84.3 (81.6, 87.0) | 0.004 | 1140 | 82.5 (80.0, 85.0) |
| Always sleeps under bed net, % | 147 | 74.5 (68.1, 81.0) | 658 | 66.4 (63.2, 69.6) | 0.03 | 805 | 67.9 (65.1, 70.8) |
| Micronutrient status | | | | | | | |
| Serum ferritin,[13] μg/L | 231 | 12.1 (10.4, 14.1) | 1136 | 21.9 (20.7, 23.1) | <0.0001 | 1367 | 19.6 (18.5, 20.7) |
| Iron deficiency,[14] % | 124 | 54.2 (46.2, 62.1) | 220 | 20.7 (17.7, 23.7) | <0.0001 | 344 | 26.9 (23.9, 30.0) |
| Serum sTfR,[13] mg/L | 231 | 11.1 (10.2, 12.1) | 1136 | 7.5 (7.3, 7.7) | <0.0001 | 1367 | 8.1 (7.9, 8.3) |
| Serum RBP,[13] μmol/L | 231 | 1.02 (0.97, 1.07) | 1136 | 1.10 (1.08, 1.12) | <0.0001 | 1367 | 1.08 (1.07, 1.10) |
| Vitamin A deficiency,[15] % | 11 | 5.0 (1.7, 8.3) | 28 | 2.6 (1.5, 3.7) | 0.1 | 39 | 3.0 (1.9, 4.1) |
| RBC folate, nmol/L | 231 | 682.5 (630.9, 738.3) | 1136 | 630.1 (611.1, 649.7) | 0.07 | 1367 | 639.5 (621.4, 658.2) |
| Risk of folate deficiency,[16] % | 13 | 8.5 (3.3, 13.6) | 57 | 5.3 (3.4, 7.2) | 0.2 | 70 | 5.9 (4.1, 7.8) |
| Serum zinc,[13] μg/dL | 231 | 76.0 (70.8, 81.7) | 1136 | 81.2 (78.7, 83.8) | 0.05 | 1367 | 80.2 (77.0, 83.6) |
| Zinc deficiency,[17] % | 59 | 24.6 (18.2, 31.1) | 252 | 20.7 (18.0, 23.5) | 0.2 | 1367 | 80.2 (78.0, 82.6) |
| Dietary and supplement intake | | | | | | | |
| Micronutrient powder intake,[18] % | 3 | 0.6 (0.0, 1.3) [5] | 20 | 2.2 (1.0, 3.3) | 0.03 | 23 | 1.9 (0.9, 2.8) |
| Prior day food consumption, % | | | | | | | |
| Flesh, organ, or blood-based foods | 49 | 21.7 (15.0, 28.5) | 341 | 28.0 (24.7, 31.4) | 0.1 | 390 | 26.9 (23.9, 29.9) |
| Legumes | 167 | 76.4 (70.3, 82.6) | 828 | 74.4 (71.2, 77.5) | 0.5 | 995 | 74.7 (71.9, 77.6) |
| Green, leafy vegetables | 59 | 28.7 (21.0, 36.5) | 434 | 36.7 (33.1, 40.2) | 0.08 | 493 | 35.2 (31.9, 38.4) |
| Vitamin A-rich fruits or vegetables | 22 | 10.0 (4.9, 15.1) | 174 | 16.8 (14.0, 19.6) | 0.05 | 196 | 15.5 (13.0, 18.0) |
| Fortified infant foods[19] | 15 | 6.9 (3.0, 10.8) | 67 | 7.0 (5.1, 8.9) | 0.9 | 82 | 7.0 (5.2, 8.7) |
| Tea or Tibetan tea | 83 | 39.5 (31.3, 47.7) | 558 | 47.6 (43.9, 51.3) | 0.08 | 641 | 46.1 (42.7, 49.5) |

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| | Anemia[2] [*n* = 231, 18.6% (95% CI: 15.8, 21.4)] | | No anemia[2] [*n* = 1136, 81.4% (95% CI: 78.6, 84.2)] | | | Total (*n* = 1367) | |
|---|---|---|---|---|---|---|---|
| | *n* | | *n* | | *P*[3] | *n* | |
| Minimum dietary diversity[20] | 96 | 46.7 (38.5, 54.9) | 548 | 47.7 (43.9, 51.5) | 0.8 | 644 | 47.5 (44.0, 51.0) |
| Consumption of foods prepared with purchased fortifiable staples,[18] % | | | | | | | |
| Maida or Aata wheat flour | 47 | 23.3 (15.6, 30.9) | 273 | 27.7 (24.2, 31.2) | 0.3 | 320 | 26.9 (23.6, 30.1) |
| Vegetable ghee | 3 | 1.0 (0.0, 2.2) [5] | 19 | 2.2 (1.1, 3.2) | 0.2 | 22 | 2.0 (1.1, 2.9) |
| Pica,[18] % | 42 | 14.9 (9.4, 20.4) | 156 | 10.1 (8.2, 11.9) | 0.07 | 198 | 11.0 (9.2, 12.8) |

[1] *ns* are unweighted. Values presented are geometric mean (95% CI) or % (95% CI). All estimates account for complex sampling design with sample weights and SAS STRATA and CLUSTER statements. AGP, α-1 acid glycoprotein; CRP, C-reactive protein; G6PD, glucose-6-phosphate dehydrogenase deficiency; sTfR, transferrin receptor; RBP, retinol-binding protein.

[2] Anemia defined as altitude-adjusted hemoglobin <11.0 g/dL (3).

[3] *P* values calculated for Rao-Scott chi-square tests (categorical) and linear contrast tests (continuous).

[4] Other Terai ethnicities include Terai/Madhesi ethnicities not including Terai/Madhesi Brahmin/Chettri (19).

[5] Interpret with caution. Estimates may be unstable because of small *n*.

[6] Water source based on caregiver report. Improved water source defined as piped water, tubewell borehole, protected well or spring, stone tap, rainwater, or bottle water (20).

[7] Hemoglobin adjusted for altitude (3).

[8] Anemia severity categorized as mild (adjusted hemoglobin 10.0–10.9 g/dL), moderate anemia (adjusted hemoglobin 70–9.9 g/dL), and severe (adjusted hemoglobin <7.0 g/dL) (3).

[9] Stunting defined as length/height-for-age *z* score <−2 SD. Underweight defined as weight-for-age *z* score <−2 SD. Wasting defined as weight-for-length/height zscore <−2 SD (14).

[10] Caregiver reported child treated for marasmus/kwashiorkor during the 12 mo preceding the survey.

[11] Soil-transmitted helminths including hookworm, *Trichuris trichura*, and *Ascaris lumbricodes*.

[12] Hemoglobinopathies include α- and β-thalassemia, hemoglobin E, and sickle cell.

[13] Biomarker was regression-adjusted to a pooled country reference to adjust for inflammation, with CRP and AGP (ferritin, RBP zinc) or AGP only (sTfR) (15).

[14] Iron deficiency defined as inflammation-adjusted serum ferritin <12.0 μg/L (3).

[15] Vitamin A deficiency defined as inflammation-adjusted serum RBP <0.69 μmol/L. To find the population-specific RBP cutoff, we regressed RBP on retinol to determine the RBP equivalent of retinol <0.70 μmol/L based on the subsample of 200 children for whom serum retinol was assessed with HPLC from the same blood draw as RBP (16).

[16] Folate cutoff based on the risk of megaloblastic anemia defined as RBC folate <305.0 nmol/L (17).

[17] Zinc deficiency defined as inflammation-adjusted serum zinc <65.0 μg/dL for nonfast, morning (i.e., before 12:00) samples and <57.0 μg/dL for nonfasted, afternoon (i.e., after 12:00) samples (18).

[18] During the 7 d preceding the survey.

[19] Fortified infant foods such as cerelac, lito from superflour, unilito, nutrimix, champion, and other fortified complementary foods.

[20] Minimum dietary diversity defined as intake from ≥4 of the 7 main food groups the day preceding the survey (12).

**TABLE 2**

Bivariate and multivariable logistic regression predicting anemia among children 6–59 mo, Nepal National Micronutrient Status Survey, Nepal, 2016 ($n$ = 1367)[1]

| | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | *P* |
|---|---|---|---|
| Age 6–23 mo (compared with 23–59 mo) | 2.89 (2.07, 4.02) | 2.29 (1.52, 3.46) | <0.0001 |
| Ecological zone (ref. Plains) | | | |
| Mountain | 0.59 (0.36, 0.94) | 0.70 (0.35, 1.42) | 0.3 |
| Hill | 0.55 (0.37, 0.81) | 0.84 (0.47, 1.49) | 0.5 |
| Ethnicity (ref. Brahmin/Chettri) | | | |
| Other Terai ethnicities[2] | 3.29 (1.80, 6.01) | 2.59 (1.25, 5.35) | 0.01 |
| Dalit | 1.31 (0.76, 2.28) | 0.98 (0.54, 1.77) | 0.9 |
| Janajati | 1.33 (0.83, 2.13) | 1.53 (0.91, 2.55) | 0.1 |
| Newar | 0.65 (0.20, 2.11) | 0.74 (0.26, 2.12) | 0.6 |
| Muslim/Other | 4.69 (2.01, 10.92) | 3.15 (1.30, 7.65) | 0.01 |
| Household wealth tertile (ref. poorest) | | | |
| Middle | 1.50 (0.97, 2.30) | 1.17 (0.66, 2.08) | 0.6 |
| Wealthiest | 0.86 (0.55, 1.35) | 0.69 (0.38, 1.26) | 0.2 |
| G6PD | 3.39 (2.31, 4.96) | 2.84 (1.88, 4.30) | <0.0001 |
| Open defecation | 1.69 (1.03, 2.77) | 0.59 (0.31, 1.14) | 0.1 |
| Stunting[3] | 1.57 (1.11, 2.22) | 1.31 (0.76, 2.26) | 0.3 |
| Underweight (ref. normal/overweight)[4] | 1.63 (1.15, 2.32) | 1.42 (0.80, 2.59) | 0.2 |
| Recent fever[5] | 1.63 (1.13, 2.35) | 1.68 (1.08, 2.59) | 0.02 |
| Recent diarrhea[6] | 1.99 (1.30, 3.02) | 1.27 (0.80, 2.02) | 0.3 |
| Always sleeps under bed net (compared with sometimes/never) | 1.48 (1.02, 2.14) | 1.04 (0.64, 1.71) | 0.9 |
| Received deworming | 0.56 (0.37, 0.83) | 0.86 (0.55, 1.34) | 0.5 |
| Micronutrient powder intake | 0.27 (0.07, 0.98) | 0.25 (0.07, 0.86) | 0.03 |
| Ln CRP in mg/L | 1.28 (1.12, 1.46) | 1.23 (1.03, 1.45) | 0.02 |
| AGP in g/L | 1.72 (1.27, 2.32) | 1.04 (0.65, 1.65) | 0.8 |
| Ln ferritin in μg/L[7] | 0.42 (0.33, 0.53) | 0.49 (0.38, 0.64) | <0.0001 |

| | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | *P* |
|---|---|---|---|
| Ln RBP in μmol/L[7] | 0.27 (0.12, 0.62) | 0.42 (0.18, 0.95) | 0.04 |

[1]Estimates are unadjusted and adjusted OR and 95% CI from bivariate and multivariable logistic regression, respectively. All variables included in the model are presented in the table. All estimates account for complex sampling design with sample weights and SAS STRATA and CLUSTER statements. Anemia was defined as altitude-adjusted hemoglobin <11.0 g/dL (WHO 2011). Candidate predictors were those where $P < 0.05$ in bivariate analyses. AGP, α-1 acid glycoprotein; CRP, C-reactive protein; G6PD, glucose-6-phosphate dehydrogenase deficiency; RBP retinol-binding protein.

[2]Other Terai ethnicities include Terai/Madhesi ethnicities not including Terai/Madhesi Brahmin/Chettri (19).

[3]Stunting defined as height/length-for-age *z* score <−2SD (14).

[4]Underweight defined as weight-for-age *z* score <−2 SD (14).

[5]Recent fever defined as caregiver report of fever during the 2 wk preceding the survey.

[6]Recent diarrhea defined as caregiver report of diarrhea during the 2 wk preceding the survey.

[7]Biomarker was regression-adjusted to a pooled country reference to adjust for inflammation, with CRP and AGP (15).