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*Article*

# Association between anemia in children 6 to 23 months old and child, mother, household and feeding indicators

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**Abstract:** In Low and Lower-Middle-Income countries, the prevalence of anemia in infancy remains high. In early childhood anemia cause irreversible cognitive deficits and represents a higher risk of child mortality. The consequences of anemia in infancy are a major barrier to overcome poverty traps. The aim of this study was to analyze based on a multi-level approach, different factors associated with anemia in children 6-23m old based on recent available Standard Demographic Health Surveys (S-DHS). We identified 52 S-DHS that had complete information in all covariates of interest in our analysis between 2005 and 2015. We performed traditional logistic regressions and multilevel logistic regression analyses to study the association between hemoglobin concentrations and household, child, maternal, socio-demographic variables. In our sample, 70 % of the 6-23m old children were anemic. Child anemia was strongly associated with maternal anemia, household wealth, maternal education and low birth weight. Children fed with fortified foods, potatoes and other tubers had significantly lower rates of anemia. Improving overall household living conditions, increasing maternal education, delaying childbearing and introducing iron rich foods at six months of age may reduce the likelihood of anemia at in toddlerhood.

**Keywords:** Anemia; infancy and toddlerhood; low and middle-income countries; Demographic and Health survey; infant feeding; multilevel regression.

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## 1. Introduction

The World Health Organization (WHO) reported that in 2011 the prevalence of anemia among 6-59 month-old children was 42.6% globally (1). The highest prevalence rates were observed in African (62.3%), South-East-Asian (53.8%) and the Eastern-Mediterranean (48.6%) regions. The adverse health consequences of anemia among pre-school children are well documented, some having an impact over a lifetime (2, 3). These include impaired cognitive development and growth, increased susceptibility to infections, fatigue and lower physical activity.

The social costs associated with anemia in early childhood are vast and largely affecting children born in lower income groups. Plessow et al. estimated that over one percent of the Indian Gross Domestic Product (GDP) is lost every year due to Iron Deficiency Anemia among 6-59-month-old children. In addition, it causes over 8 million Disability Adjusted Life Years (DALYs) lost and affects disproportionally younger infants from lower wealth households (4). Over 95 % of this economic and 80% of the health burden was linked to children 6 to 23 months of age.

The most frequent factors associated with anemia among children are malnutrition and infections (5). According to the WHO globally approximately half of the anemia is linked to iron deficiency, although this proportion varies by geography and population groups (1, 6). Other

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conditions can also lead to anemia, such as a deficiency of other micronutrients, phytate rich diets, acute and chronic infections including malaria, HIV and tuberculosis, as well as hemoglobinopathies (7-9).

In addition maternal, household and community factors have been reported to increase the risk of being anemic in early childhood. The complexity of these factors and their interaction require multi-faceted strategies to address anemia globally. However, it is difficult to draft optimal policies without untangling the relative contribution of these factors associated with increased risk of anemia and their inter-relation.

Anemia among infants is determined by a large number of factors. For example, poverty per se leads to increased food insecurity and lower sanitation facilities, but could only be considered as the cause of anemia indirectly. It acts through inter-related determinants (intermediate variables). These intermediate determinants can be further divided into hierarchically or parallel inter-related sub-groups. Victora et al. proposed the use of conceptual frameworks in epidemiological multivariate analysis (10). They postulate that multivariate analysis is most often used to determine the effect of an assumed risk factor on the investigated outcome after controlling for cofounding factors to explore whether the effect is direct or mediated by other factors. Researchers often combine multi-level modeling with epidemiological conceptual frameworks to analyze confounders at different levels of data clustering. Uthman and Ngnie-Teta et al. used both multi-level modeling and conceptual frameworks. The first to analyze factors associated with child malnutrition in Nigeria, and the second to analyze the individual and community variables associated with the severity of anemia in children in Mali and Benin (6, 11). Merlo et al. had extensively discussed the advantages and limitations of multi-level analysis in social epidemiology in dichotomous dependent variables (12, 13). Among the advantages of using multilevel regression discussed by Merlo are that this technique provides additional understanding of the distribution and determinants of geographical, social, and individual disparities in health status.

In our analysis, we adopt this multi-level approach to explore the key risk factors, malnutrition and infections, in childhood anemia globally adding a detailed analysis on the role of the consumption of different food groups.

## 2. Materials and Methods

### *2.1. Study question*

The primary objectives of this analysis is to understand the relative importance of the countries' human development, the geographical regions, community, household, maternal, child and nutritional variables in relation to the prevalence of anemia between the age of 6 and 23 months. We have a special interest to explore how anemia can be associated to the intake of different food groups as, both Global Alliance for Improved Nutrition (GAIN) and the Scaling Up Nutrition (SUN) framework acknowledge the importance of iron fortification of foods in reducing the risk of anemia (14-16).

### *2.2. Data and study population*

We used publicly available data from the Standard Demographic Health Survey (DHS) [USAID http://dhsprogram.com/] that was collected from 2005 to 2016 in Asia, North-Africa, the Middle East, Sub-Saharan Africa and Latin America. We originally identified 104 accessible standard DHS in the period of interest. However, we only kept the surveys that had information on hemoglobin and the covariates of interest. The final sample consisted of 52 surveys from 41 countries with over 136 thousand children from six to 23 months of age. The surveys included in this analysis are listed in the Appendix Table A1. DHS are national representative household surveys with primary focus on women 15 to 49 years old and children under 5 years old. The surveys had information about the health of each woman and her children as well as demographics and socioeconomics. Importantly, the DHS also includes a section on all foods that the woman's youngest child was given in the past 24 h.

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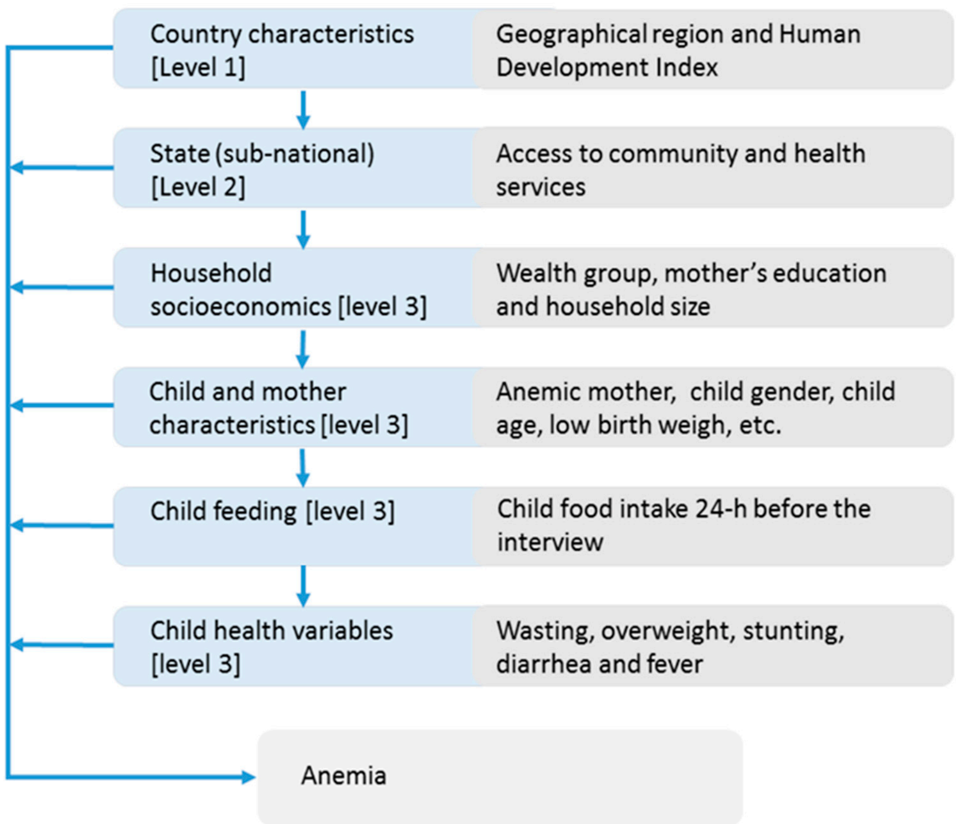
*2.3. Study variables*

The outcome variable was anemia defined by hemoglobin concentration adjusted by altitude using the anemia threshold proposed by WHO for infants that is below 110 g/L (17). We decided to use anemia as a dichotomous variable instead of using a continuous hemoglobin concentration because odds ratios are directly interpretable. DHS collects hemoglobin data using the HemoCue system, which consists of a device that estimate hemoglobin concentrations from blood samples obtained in the field using finger prick (or heel prick), and yields results comparable to those obtained from other test systems (18).

Figure 1 presents the conceptual framework used in the analysis to describe the hierarchical and inter-related nature of the various determinants contributing to infant anemia. The framework proposed here extends the one used by Ngnie-Teta et al. The framework considers the development level of the geographic region because of the global nature of the analysis, as well as a better understanding of the potential role of the food intake (6). Food intake from cross-sectional data can only be analyzed in relation to health outcomes with large sample sizes, as there are many limitations in a cross-sectional data structure that are only partially overcome with larger samples. DHS only provides food intake information from a 24-hour feeding questionnaire addressing a limited number of food groups. The arrows indicate in a simplified way how a group of determinants can influence other group variables.

Figure 1. The hierarchy of the determinants of infant anemia - conceptual framework for the multilevel analysis



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We considered a three level hierarchical model in our analysis. The first level corresponds to country characteristics that include the Human Development Index (HDI) classification at the time of the survey and the world region. Level 2 encompasses variables that classify sub-national entities (e.g. state or province) within a country based on the percentage of urban population and availability of health and community services. We measure accessibility to health care services as the percentage of infants' mothers that had at least one antenatal visit during pregnancy and infants who had undergone a medical check-up before the 2 months of age. Accessibility to community services based on the percentage of household with electricity and piped water.

The Level 3, individual variables were classified into four groups: "household socioeconomic variables", "infant and mother individual variables", "Food intake variables" and "infant's health status variables".

Household socioeconomic variables included wealth index based on housing conditions and household's assets, the mother's level of education, and household size parameters. We created dichotomous variables to distinguish households where there were six or more residents and anther variable to identify households with three children or more under the age of five. Mother and child indicators included mother's age at first birth (young mother first pregnancy at age < 18 years yes/no), maternal anemia, mother's short stature (<150 cm) (19), child age, split into three-monthly sub-groups as 6-8, 9-11, 12-14, 15-17, 18-20, 21-23 months, low birth weight (yes/no) and gender (female). Child feeding variables corresponds to the assessment of the consumption of 11 food groups by the child in the 24 hours before the interview. The 11 food-groups in the analysis are "breast milk", "fortified milks", "other milks", "fortified baby food", "foods made out of grains", "potatoes & other tubers", "fruits & vegetables", "meat, poultry, fish, eggs", "dried beans, peas, lentils, nuts", "other dairy products" and "other solid-semisolid food". The food groups correspond to the food categories asked in the standard DHS questioner in rounds 5 and 6. In some surveys, there are more granularity on the food grouping. However, we collapsed the food groups to be consistent to surveys with a more generic food grouping in the sample. The child health and nutritional indicators are: growth retardation defined as height for age z-score (HAZ) lower than minus two standard deviation (<-2SD), wasting defined as weight for height z-score (WHZ) <-2SD and overweight defined as WHZ>+2SD(20). In addition, number of fever and diarrhea cases during the two weeks previous to survey interview were included.

*2.4. Data analysis method*

The inclusion criteria for the explanatory variables in the analysis were based on previous studies on child anemia and the availability of the variables in the DHS surveys. To verify the statistical relevance of the selected variables before inclusion in the multivariate models we ran univariate regression. Variables that were not significantly associated with anemia or were not reported in a comparable way across surveys were excluded from the subsequent regression analysis.

In this global analysis, we estimated the odds ratio between anemia in children 6 to 23 months old and the explanatory variables from three different procedures. First, from independent simple logistic regressions between anemia and each explanatory variable. Second, from a multivariate traditional logistic regression with all individual level variables and using fixed effects for upper level factors. Third, from a multi-level logistic regression model. The multi-level model incorporated the explanatory variables grouped at the different levels of the hierarchy in line with the conceptual framework (Figure 1). For all statistical estimations, we used Stata 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP.).

The random effect multi-level analysis allowed us to estimate variance partition coefficients (VPC) from which we estimated the inter class correlation (ICC). The ICC allows us to estimate how much of the variation is explained by clustering the data (21). A high ICC would reflect a high clustering of anemia prevalence at the national and subnational levels. We ran seven models to

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compare the changes on the ICC from adding additional groups of variables. The first model, the model 0 or null model, we only model the variance level structure specifying the levels without including any type of explanatory variables. In each subsequent model, from model 1 to model 6, we added gradually an additional group of explanatory variables as described above. Additional, we estimated the incremental explanatory power added to the regression based on log-likelihood function to estimate the contribution relative contribution of the individual level group of variables.

## 3. Results

The prevalence of anemia in our sample of 136,024 children 6 to 23 months old was 70%, with the highest prevalence of 76% in the Sub-Saharan Africa and the lowest prevalence of 45% in the North Africa and Middle East surveys. The Latin American surveys registered an anemia prevalence of 59% and the Asian surveys 70%. We present further descriptive data of our sample in Appendix Table A2.

### *3.1. Multivariate and multilevel models*

In Table 1, we display estimated odds ratios with a 95% confidence intervals (CI) and p-values from traditional logistic regression (TLR, multivariate) and the multi-level logistic regression (MLR). We could not include national and subnational variables in the TRL estimation due to collinearity as country and at state (subnational administrative divisions), heterogeneity is modeled with fixed effects. In contrast, in the MLR estimation, we were able to include country and state variables because the clustering effect is assumed to be random. We described in the following text the results of the MLR model. In the next section, we discuss the difference between both estimates.

At the country level variables, we found that children living in countries with higher HDI (above the 0.55 threshold for lower-middle class) had 29% lower odds of being anemic than those living in less developed countries and remains statistically significant. By region, no significant difference was found once we controlled for all covariates based on 52 groups (surveys). Subnational level variables urbanity, access to health care services and access to community services failed to have a statistical significant estimator once considering all covariates.

Most of the individual level variables remained significant after taking into account all covariates. In the household socioeconomic variables group, wealth index was a strongly associated with child anemia. Children born in households at the fifth wealth quintile had a 27% lower odds of being anemic compared with the peers in the first quintile (OR 0.73 95%CI: 0.69 -0.76). In the same direction, children from mother mothers with secondary education or higher (OR 0.82, 95%CI: 0.78 - 0.85) and living in household with three or less children (OR 1.07, 95%CI: 1.03 - 1.11) were significantly less likely to be anemic. For mother and infant variables, we found that maternal anemia (OR 1.69, 95%CI: 1.65 - 1.74) and child low birth weight (OR 1.16, 95%CI: 1.12 - 1.19) were associated with lower anemia rates. Girls (OR 0.89, 95%CI: 0.86 - 0.91) were less likely to be anemic than boys. Anemia and age had an inverted U pattern from six to 23 months of age. Anemia was significantly higher in children from 12 to 14 months old (OR 1.07, 95%CI: 1.02 - 1.11) while significantly lower at 21 to 23 months of age (OR 0.74, 95%CI: 0.70 - 0.77) compared to the base line group from six to eight months of age. In the feeding variables groups, only fortified milks (OR 0.86, 95%CI: 0.82 - 0.90), fortified baby food (OR 0.90, 95%CI: 0.87 - 0.94) and tubers (OR 0.96, 95%CI: 0.93 - 0.98) were significantly associated with lower anemia rates. Consumption of foods made from grains, mainly in form of homemade porridge, bread or noodles was associated with higher anemia rates (OR 1.09, 95%CI: 1.05 - 1.12). Breastmilk was associated with higher anemia rates (OR 1.07, 95%CI: 1.04 - 1.11) in the multilevel regression but it was not significant in the traditional logistic regression. Child's health variables were significantly associated with higher anemia rates: wasting (OR 1.08, 95%CI: 1.04 - 1.12), stunting (OR 1.20, 95%CI: 1.16 - 1.23), diarrhea (OR 1.05, 95%CI: 1.01 - 1.08) and fever (OR 1.09, 95%CI: 1.06 - 1.13).

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**Table 1.** Estimated odds ratios traditional logistic and multilevel logistic regressions on anemia in children 6 to 23 months old.

| | Adjusted TLR OR (95% CI) | *p* | Adjusted MLR OR (95% CI) | *p* |
|---|---|---|---|---|
| ***Country level factors*** | | | | |
| HDI at the time of the survey | | | | |
| *Low* | | | 1 | |
| *Lower middle/ middle* | | | 0.71 (0.50 - 0.99) | 0.045 |
| World region | | | | |
| *Asia* | | | 1 | |
| *North Africa and Middle East* | | | 0.52 (0.25 - 1.11) | 0.090 |
| *Sub-Saharan Africa* | | | 1.35 (0.94 - 1.93) | 0.099 |
| *Latin America* | | | 0.89 (0.55 - 1.42) | 0.620 |
| ***Sub-national level factors*** | | | | |
| Type of residence | | | | |
| *Rural* | | | 1 | |
| *Urban* | | | 1.15 (0.96 - 1.38) | 0.122 |
| Access to health services | | | | |
| *Low* | | | 1 | |
| *High* | | | 0.94 (0.83 - 1.07) | 0.368 |
| *Access to community services* | | | | |
| *Low* | | | 1 | |
| *High* | | | 0.92 (0.80 - 1.05) | 0.222 |
| ***Socio-economic variables*** | | | | |
| Wealth quintile | | | | |
| *Lowest* | 1 | | 1 | |
| *Lower* | 0.92 (0.86 - 0.99) | 0.019 | 0.95 (0.92 - 0.99) | 0.011 |
| *Middle* | 0.91 (0.84 - 0.99) | 0.027 | 0.91 (0.88 - 0.95) | <0.001 |
| *High* | 0.88 (0.79 - 0.98) | 0.016 | 0.85 (0.81 - 0.89) | <0.001 |
| *Highest* | 0.80 (0.70 - 0.91) | <0.001 | 0.73 (0.69 - 0.76) | <0.001 |
| Household size | | | | |
| *Less than 6 members* | 1 | | 1 | |
| *6 or more members* | 1.03 (1.00 - 1.06) | 0.042 | 1.00 (0.97 - 1.02) | 0.826 |
| Children under 5 | | | | |
| *3 or less* | 1 | | 1 | |
| *More than 3* | 1.09 (1.05 - 1.14) | <0.001 | 1.07 (1.03 - 1.11) | <0.001 |
| Mother education | | | | |
| *None* | 1 | | 1 | |
| *Primary* | 0.86 (0.82 - 0.91) | <0.001 | 0.91 (0.88 - 0.95) | <0.001 |
| *Secondary and above* | 0.74 (0.70 - 0.80) | <0.001 | 0.82 (0.78 - 0.85) | <0.001 |

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**Table 1** (cont.). Estimated odds ratios traditional logistic and multilevel logistic regressions.

| | Adjusted TLR OR (95% CI) | *p* | Adjusted MLR OR (95% CI) | *p* |
|---|---|---|---|---|
| ***Mother and child variables*** | | | | |
| Mother's age at first birth | | | | |
| *18 years old and older* | 1 | | 1 | |
| *Younger than 18 years old* | 1.05 (1.01 - 1.10) | 0.021 | 1.06 (1.02 - 1.10) | <0.001 |
| Mother with anemia | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.78 (1.68 - 1.89) | <0.001 | 1.69 (1.65 - 1.74) | <0.001 |
| Stunted mother | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.00 (0.96 - 1.04) | 0.897 | 1.02 (0.99 - 1.05) | 0.147 |
| Child's low birth weight | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.20 (1.15 - 1.26) | <0.001 | 1.16 (1.12 - 1.19) | <0.001 |
| Child's gender | | | | |
| *Boy* | 1 | | 1 | |
| *Girl* | 0.89 (0.86 - 0.92) | <0.001 | 0.89 (0.86 - 0.91) | <0.001 |
| Child's age | | | | |
| *6 to 8 months* | 1 | | 1 | |
| *9 to 11 months* | 1.06 (1.00 - 1.12) | 0.061 | 1.06 (1.01 - 1.10) | 0.015 |
| *12 to 14 months* | 1.06 (0.99 - 1.14) | 0.075 | 1.07 (1.02 - 1.11) | 0.005 |
| *15 to 17 months* | 0.98 (0.88 - 1.10) | 0.778 | 0.99 (0.94 - 1.03) | 0.563 |
| *18 to 20 months* | 0.88 (0.78 - 1.00) | 0.045 | 0.87 (0.83 - 0.91) | <0.001 |
| *21 to 23 months* | 0.74 (0.64 - 0.86) | <0.001 | 0.74 (0.70 - 0.77) | <0.001 |
| Child's birth order | | | | |
| *Second or later* | 1 | | 1 | |
| *First child* | 1.03 (0.99 - 1.06) | 0.149 | 1.02 (0.99 - 1.05) | 0.231 |

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**Table 1** (cont.)**.** Estimated odds ratios traditional logistic and multilevel logistic regressions.

| | Adjusted TLR OR (95% CI) | *p* | Adjusted MLR OR (95% CI) | *p* |
|---|---|---|---|---|
| ***Child feeding variables*** | | | | |
| Breast milk | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.05 (0.98 - 1.12) | 0.170 | 1.07 (1.04 - 1.11) | <0.001 |
| Fortified milks | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.83 (0.78 - 0.89) | <0.001 | 0.86 (0.82 - 0.90) | <0.001 |
| Other milks | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.09 (1.03 - 1.16) | 0.003 | 1.00 (0.97 - 1.03) | 0.965 |
| Fortified baby food | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.86 (0.81 - 0.92) | <0.001 | 0.90 (0.87 - 0.94) | <0.001 |
| Foods made from grains | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.10 (1.05 - 1.16) | <0.001 | 1.09 (1.05 - 1.12) | <0.001 |
| Potatoes & other tubers | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.94 (0.90 - 0.99) | 0.009 | 0.96 (0.93 - 0.98) | 0.002 |
| Meat, poultry, fish, eggs | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.91 (0.84 - 0.98) | 0.011 | 0.99 (0.96 - 1.03) | 0.756 |
| Fruits and vegetables | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.97 (0.93 - 1.00) | 0.077 | 1.00 (0.97 - 1.03) | 0.825 |
| Dried beans, peas and nuts | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.97 (0.92 - 1.01) | 0.148 | 1.02 (0.98 - 1.05) | 0.410 |
| Other dairy products | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.08 (1.00 - 1.15) | 0.040 | 1.02 (0.98 - 1.05) | 0.410 |
| Other solid-semisolids foods | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.92 (0.88 - 0.96) | <0.001 | 0.99 (0.96 - 1.02) | 0.688 |

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**Table 1** (cont.)**.** Estimated odds ratios traditional logistic and multilevel logistic regressions.

| | Adjusted TLR OR (95% CI) | *p* | Adjusted MLR OR (95% CI) | *p* |
|---|---|---|---|---|
| ***Child's health variables*** | | | | |
| Wasting (WHZ<-2SD) | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.15 (1.09 - 1.22) | <0.001 | 1.08 (1.04 - 1.12) | <0.001 |
| Overweight (WHZ>+2SD) | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 0.83 (0.77 - 0.90) | <0.001 | 0.84 (0.78 - 0.90) | <0.001 |
| Stunting (HAZ<-2SD) | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.23 (1.18 - 1.28) | <0.001 | 1.20 (1.16 - 1.23) | <0.001 |
| Diarrhea in last two weeks | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.08 (1.03 - 1.13) | 0.001 | 1.05 (1.01 - 1.08) | 0.007 |
| Fever in last two weeks | | | | |
| *No* | 1 | | 1 | |
| *Yes* | 1.11 (1.07 - 1.16) | <0.001 | 1.09 (1.06 - 1.13) | <0.001 |

### *3.2. Interclass correlation and explained variance*

In the multi-level analysis, we estimated the interclass correlation, and the within country variability (community) as we introduce the different levels in the multivariate analysis. Figure 2 shows that 11% and 15% of the variability is attributable to differences between countries and states (or other subnational administrative division among countries). The interclass correlations decreases as additional groups of variables are introduced into the model. In the full model, the interclass correlation stands at 9% and 5.7% percent for the national and subnational level respectively

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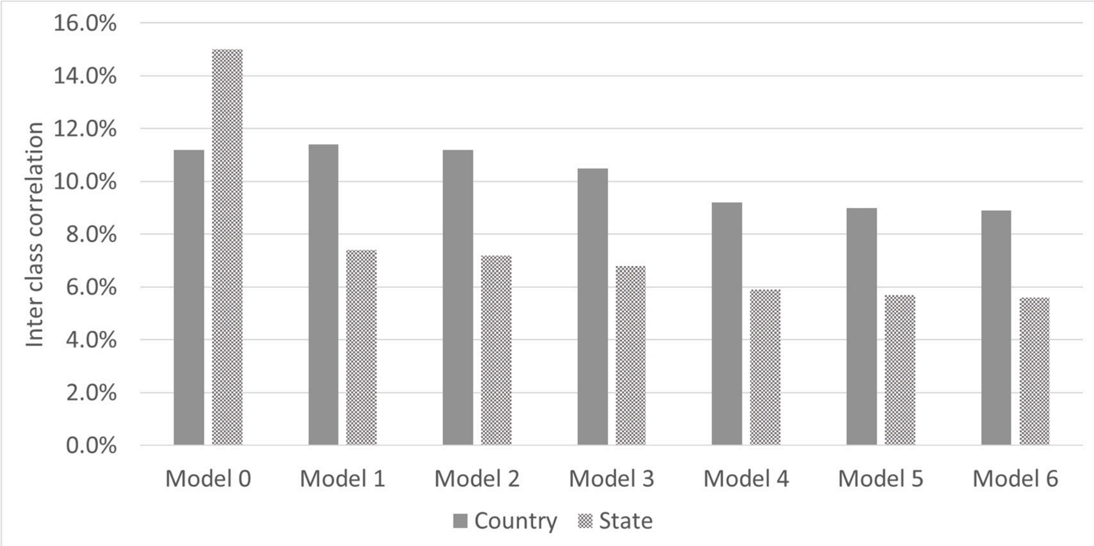
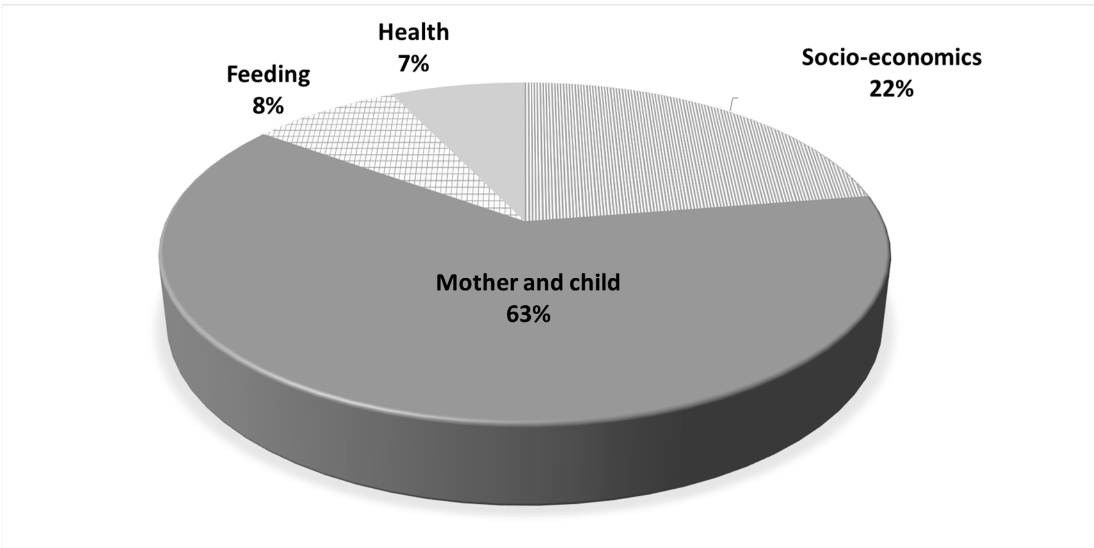



**Figure 2.** Inter class correlation by models. Model 0: Null model only variance level cluster; Model 1: adds national level variables; Model 2: adds state (subnational) level variables; Model 3: adds household socioeconomic variables; Model 4: adds child and mother characteristics; Model 5: adds feeding variables; Model 6: adds child health variables.

In Figure 3, we present the contribution of individual level variables to the total explanatory power of the model. The mother and child variable groups contributed 63% of the incremental pseudo R2. Socioeconomic variables accounted for 22% of the incremental explanatory power of the model whereas feeding variables and health variables contributed 8% and 7% respectively.

**Figure 3.** Contribution of individual level variables group to the incremental explanatory power of the regression (Pseudo R2).



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## 4. Discussion

This research pools data from DHS undertaken in Asia, Middle East, North Africa, Sub-Saharan Africa and Latin America. This is the first study that combines over 50 national surveys in low-and-lower-middle-income countries with a sample size surpassing 100 thousand children to shed some light on the association between anemia and related factors using MLR and TRL regression techniques. We found that the estimations with both approaches were very similar for all individual level variables except for the feeding variables group. In the feeding variables group some of the coefficients that were significant under the MLR were not significant at the TRL or vice versa, although the associations were consistently in the same direction. Ngnie-Teta et al. did a similar comparison on MLR and TRL using DHS from Benin and Mali and did not found major differences among the estimated coefficients using either approach (6). One possible explanation for these differences could be due to the nature of these variables. The effect of food types could partially be indirect (intermediate variables). Our estimates of the interclass correlations, once we control by full covariates, were relatively low, 9% at national level and 5.7% at subnational level.

As expected, higher level of HDI were significant associated with lower prevalence of anemia even after controlling for other variables. State level variables were not statistically significant after controlling for the full variables of the model. This may indicate that community variables probably are also reflected in socioeconomic and other individual variables thus their statistical power is diluted. Household socioeconomic variables are good predictors of the likelihood of anemia in children at this age in line with previous literature (22). Child and mother variables had the highest incremental explanatory power with maternal anemia coefficient being the greatest in magnitude. The strong association between maternal and child anemia could be due to many factors that determine anemia that are share between mother and child (22, 23). Age groups coefficients were statistically significant suggesting an inverted-U-pattern between the prevalence of anemia and age in months. (24-26).

Few coefficients from the feeding variable groups were statistically significant. Nonetheless, it is not surprisingly that among the food groups fortified milks and fortified baby foods had the strongest significant association with lower anemia rates as there is a biochemical pathway supported by several clinical trials (15, 16). Cross-association between feeding groups and health outcomes such anemia may reflect a causal relationship between nutrient density content of the foods and the specific impact on health outcome (27). Nonetheless, because food consumption was assessed a day before that the anemia measurement was taken, a significant association could be pointing at persistent feeding habits. Randomized Clinical Trials (RCTs) have shown a positive effect of iron fortified products on hemoglobin after 4 to 6 months of regular consumption. Therefore, a contemporaneous association between feeding habits and hemoglobin or anemia requires that current and past consumption patterns to be highly correlated to potentially reflect the possible causal path on nutrient density of the foods and health outcomes. Food made out of grains, including homemade porridges (no fortified), bread and noodles, had a statistical significantly association with anemia. This association could arise because these foods could replace other iron-rich foods in the diet or the presence of phytic acids that reduce the absorption of iron (28). Breastmilk had no clear association with anemia, in the TLR the association was not significant while it was negatively associated with anemia in MLR. Breastmilk contains very little amounts of iron and if the mothers diet is not diversified breastmilk would not contribute enough to meet the infants daily iron requirements (29-31). However, on the other hand breastmilk prevents infections that could cause anemia (32).

The associations between anemia and health variables are in the expected direction according to the previous literature (5, 22). Wasting and stunting were significantly associated with higher anemia prevalence. Similar to anemia, wasting and stunting are cause by caused by long-term insufficient nutrient intake and frequent infections. The inclusion of wasting and stunting may reduce the omitted variable bias on other parameters as we take indirectly into consideration environmental factors and dietary diversity in the past. Fever and diarrhea result frequently from infectious diseases

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such as malaria. In the absence of malaria controlling variables in this study such as bed nets and malaria testing these variables could improve the estimates.

This study has a number of limitations. First, using cross sectional data prevented us to do any causal inference. As discussed above, some associations reflect a causal pathway but we do not have the appropriate data structure to support this. Second, our data are from various geographies, therefore our estimates represent an average of our sample that may differ between countries in the sample. However, our estimates are aligned with the previous findings in the literature and highlight future areas of interest for additional studies. Increasing our sample by increasing the total number of surveys came at a cost of limiting the number of variables analyzed such as excluding measures of bed nets or prevalence of malaria. Although few DHS have information on this, most DHS focus more on other child and maternal aspects.

## 5. Conclusions

The prevalence of anemia during the complementary feeding in low and lower-middle-income countries remains high. This is a critical period in life as the anemia during this age could lead to improper child neurodevelopment. Around two thirds of the children at six month of age in our sample were anemic, early life interventions should be prioritize to reduce the likelihood of being anemic at that age. Improving overall household living conditions as well as increasing maternal education, delaying and spacing childbearing and introducing iron rich foods in weaning (33) could also have a positive impact on reducing anemia in infancy. Public health program should target infants from anemic mothers and infants in deprived households as they are at higher risk of anemia. Given the association between fever and diarrhea with anemia, reducing infection diseases, through sanitation, vaccination and malaria prevention could enhance hemoglobin concentrations.

**Author Contributions:** APP conceptualized the framework analysis, ran the data analysis, drafted and revised the paper; PRD provided inputs for the data analysis, drafted and revised the paper; KVH and ZH, provided inputs for the analysis, drafted and revised the paper.

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**Conflicts of Interest:** Dr. Prieto Patron, Dr. Detzel, Dr. Hutton are employed by Nestec SA, Nestlé Research Center. Klazine Van Der Host previously has worked for Nestlé research.

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## Appendix A

**Table A1.** Countries and years in sample.

| World region | Country and survey year in parenthesis |
|---|---|
| Asia (11 surveys) | Azerbaijan (2006); Bangladesh (2011); Cambodia (2010, 2014); India (2005, 2015); Kyrgyzstan (2012); Myanmar (2015); Nepal (2006, 2011); Timor-Leste (2009) |
| North-Africa & Middle-East (2 surveys) | Egypt (2014); Jordan (2012) |
| Sub-Saharan Africa (33 surveys) | Benin (2006, 2011); Burkina Faso (2010); Burundi (2010); Cameroon (2011); Congo (2011); Dem. Rep. Congo (2013); Cote d'Ivoire (2011); Ethiopia (2011); Gabon (2012); Gambia (2013); Ghana (2014); Guinea (2012); Lesotho (2014); Malawi (2010, 2015); Mali (2012); Mozambique (2011); Namibia (2013); Niger (2012); Rwanda (2010, 2014); São Tomé and Príncipe (2008); Senegal (2010); Sierra Leone (2008, 2013); Swaziland (2006); Tanzania (2015); Togo (2013); Uganda (2006); Zimbabwe (2005, 2010, 2015) |
| Latin-America (6 surveys) | Guatemala (2014); Guyana (2009); Haiti (2005, 2012); Honduras (2005, 2011) |

**Table 2.** Descriptive statistics of the sample.

| | *Asia* | *North Africa and Middle East* | *Sub-Saharan Africa* | *Latin America* | *Total* |
|---|---|---|---|---|---|
| ***Dependent variable*** | | | | | |
| Anemia | 70.1% | 44.9% | 75.6% | 58.6% | 70.2% |
| ***Country and community variables*** | | | | | |
| HDI at the time of the survey | 81.9% | 100.0% | 9.7% | 81.9% | 61.5% |
| Mostly urban state | 3.9% | 74.6% | 12.0% | 21.1% | 9.4% |
| Access to community services | 53.7% | 100.0% | 6.3% | 71.6% | 42.6% |
| Access to health care | 41.9% | 100.0% | 77.8% | 92.7% | 57.9% |

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**Table A2** (cont.). Descriptive statistics of the sample.

| | *Asia* | *North Africa and Middle East* | *Sub-Saharan Africa* | *Latin America* | *Total* |
|---|---|---|---|---|---|
| ***Household, mother and child variables*** | | | | | |
| Household size | | | | | |
| *6 or more members* | 57.9% | 43.8% | 58.% | 54.2% | 57.3% |
| *More than 3 children U5* | 16.4% | 18.3% | 24.8% | 15.5% | 18.8% |
| Maternal education | | | | | |
| *No education* | 28.8% | 7.9% | 36.3% | 13.6% | 29.2% |
| *Primary education* | 15.5% | 6.9% | 37.5% | 57.% | 25.2% |
| *Secondary or higher* | 55.7% | 85.2% | 26.2% | 29.4% | 45.7% |
| Mother younger than 18 years old | 12.8% | 8.% | 33.% | 33.4% | 20.3% |
| Mother with anemia | 55.6% | 30.6% | 38.3% | 21.9% | 47.2% |
| Low birth weight child | 31.4% | 20.9% | 17.3% | 19.5% | 26.1% |
| Female child | 47.9% | 47.4% | 50.% | 48.6% | 48.5% |
| Frist born child | 36.3% | 24.9% | 22.4% | 31.9% | 31.7% |
| ***Child feeding variables*** | | | | | |
| Breast milk | 84.8% | 52.8% | 82.1% | 74.1% | 82.3% |
| Fortified milks | 9.8% | 5.7% | 5.7% | 9.5% | 8.5% |
| Other milks | 39.7% | 49.5% | 15.6% | 33.8% | 32.5% |
| Fortified baby food | 14.4% | 7.6% | 9.5% | 27.8% | 13.9% |
| Foods made from grains | 68.3% | 73.9% | 65.5% | 81.8% | 68.8% |
| Potatoes & other tubers | 32.% | 44.9% | 32.6% | 46.% | 33.6% |
| Meat, poultry, fish, eggs | 20.7% | 57.6% | 41.7% | 66.2% | 31.5% |
| Fruits and vegetables | 43.3% | 58.9% | 49.3% | 55.4% | 46.4% |
| Dried beans, peas and nuts | 15.1% | 18.2% | 21.9% | 58.1% | 20.8% |
| Other dairy products | 15.5% | 67.3% | 9.1% | 34.9% | 16.5% |
| Other solid-semisolids foods | 25.% | 45.5% | 42.7% | 54.3% | 33.% |
| ***Child's health variables*** | | | | | |
| Wasting (WHZ<-2SD | 21.8% | 7.2% | 11.2% | 3.3% | 16.9% |
| Overweight (WHZ>+2SD) | 6.3% | 19.3% | 11.7% | 14.7% | 8.9% |
| Stunting (HAZ<-2SD) | 34.4% | 12.5% | 29.6% | 27.7% | 31.9% |
| Diarrhea in last two weeks | 15.1% | 24.5% | 25.8% | 29.9% | 19.6% |
| Fever in last two weeks | 18.8% | 27.% | 27.4% | 29.7% | 22.4% |
| *Number of observations* | 82 343 | 3 231 | 39 440 | 11 529 | 136 543 |

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Peer-reviewed version available at Nutrients 2018, 10, 1269; doi:10.3390/nu10091269

## References


1. WHO. The global prevalence of anaemia in 2011. WHO, 2015.
2. Lozoff B, Beard J, Connor J, Felt B, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. Nutrition reviews. 2006;64(suppl_2):S34-S43.
3. Walker SP, Wachs TD, Gardner JM, Lozoff B, Wasserman GA, Pollitt E, et al. Child development: risk factors for adverse outcomes in developing countries. The lancet. 2007;369(9556):145-57.
4. Plessow R, Arora NK, Brunner B, Tzogiou C, Eichler K, Brugger U, et al. Social Costs of Iron Deficiency Anemia in 6-59-Month-Old Children in India. PloS one. 2015;10(8):e0136581.
5. Stephenson LS, Latham MC, Ottesen E. Malnutrition and parasitic helminth infections. Parasitology. 2000;121(S1):S23-S38.
6. Ngnie-Teta I, Receveur O, Kuate-Defo B. Risk factors for moderate to severe anemia among children in Benin and Mali: insights from a multilevel analysis. Food and nutrition bulletin. 2007;28(1):76-89.
7. Zimmermann MB, Hurrell RF. Nutritional iron deficiency. The Lancet. 2007;370(9586):511-20.
8. Dreyfuss ML, Stoltzfus RJ, Shrestha JB, Pradhan EK, LeClerq SC, Khatry SK, et al. Hookworms, malaria and vitamin A deficiency contribute to anemia and iron deficiency among pregnant women in the plains of Nepal. The Journal of nutrition. 2000;130(10):2527-36.
9. Lanzkowsky P. Classification and diagnosis of anemia in children. Lanzkowsky's Manual of Pediatric Hematology and Oncology (Sixth Edition): Elsevier; 2016. p. 32-41.
10. Victora CG, Huttly SR, Fuchs SC, Olinto M. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. International journal of epidemiology. 1997;26(1):224-7.
11. Uthman OA. A multilevel analysis of individual and community effect on chronic childhood malnutrition in rural Nigeria. Journal of tropical pediatrics. 2008;55(2):109-15.
12. Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. Journal of Epidemiology & Community Health. 2006;60(4):290-7.
13. Merlo J, Yang M, Chaix B, Lynch J, Råstam L. A brief conceptual tutorial on multilevel analysis in social epidemiology: investigating contextual phenomena in different groups of people. Journal of Epidemiology & Community Health. 2005;59(9):729-36.
14. Nutrition SU. Scaling up nutrition: a framework for action. Washington, DC: UNSCN. 2010.
15. Eichler K, Wieser S, Rüthemann I, Brügger U. Effects of micronutrient fortified milk and cereal food for infants and children: a systematic review. BMC public health. 2012;12(1):506.
16. Das JK, Salam RA, Kumar R, Bhutta ZA. Micronutrient fortification of food and its impact on woman and child health: a systematic review. Systematic Reviews. 2013;2(1):67.
17. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva, Switzerland: World Health Organization; 2011. Contract No: WHO/NMH/NHD/MNM/111. 2014.
18. Bäck S-E, Magnusson CG, Norlund LK, von Schenck HH, Menschik ME, Lindberg PES. Multiple-site analytic evaluation of a new portable analyzer, HemoCue Hb 201+, for point-of-care testing. Point of Care. 2004;3(2):60-5.
19. Subramanian S, Ackerson LK, Smith GD, John NA. Association of maternal height with child mortality, anthropometric failure, and anemia in India. Jama. 2009;301(16):1691-701.
20. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF. NCHS growth curves for children birth-18 years. Department of Health Education and Welfare Washington, D.C., 1977.
21. Rabe-Hesketh S, Skrondal A. Multilevel and longitudinal modeling using Stata: STATA press; 2008.
22. Pasricha S-R, Black J, Muthayya S, Shet A, Bhat V, Nagaraj S, et al. Determinants of anemia among young children in rural India. Pediatrics. 2010;126(1):e140-e9.
23. de Pee S, Bloem MW, Sari M, Kiess L, Yip R, Kosen S. The high prevalence of low hemoglobin concentration among Indonesian infants aged 3–5 months is related to maternal anemia. The Journal of nutrition. 2002;132(8):2215-21.
24. Lutter CK. Iron deficiency in young children in low-income countries and new approaches for its prevention. The Journal of nutrition. 2008;138(12):2523-8.
25. Chaparro CM, Neufeld LM, Alavez GT, Cedillo RE-L, Dewey KG. Effect of timing of umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. The Lancet. 2006;367(9527):1997-2004.

*Preprints* (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 July 2018 doi:10.20944/preprints201807.0130.v1

Peer-reviewed version available at *Nutrients* **2018**, *10*, 1269; doi:10.3390/nu10091269

26. Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. Jama. 2007;297(11):1241-52.
27. Bhargava A. Food, economics, and health: Oxford University Press Oxford:; 2008.
28. Teucher, Olivares, Cori. Enhancers of iron absorption: ascorbic acid and other organic acids. International journal for vitamin and nutrition research. 2004;74(6):403-19.
29. Meinzen-Derr JK, Guerrero ML, Altaye M, Ortega-Gallegos H, Ruiz-Palacios GM, Morrow AL. Risk of infant anemia is associated with exclusive breast-feeding and maternal anemia in a Mexican cohort. The Journal of nutrition. 2006;136(2):452-8.
30. Calvo EB, Galindo AC, Aspres NB. Iron status in exclusively breast-fed infants. Pediatrics. 1992;90(3):375-9.
31. Pizarro F, Yip R, Dallman PR, Olivares M, Hertrampf E, Walter T. Iron status with different infant feeding regimens: relevance to screening and prevention of iron deficiency. The Journal of pediatrics. 1991;118(5):687-92.
32. Duijts L, Jaddoe VW, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. Pediatrics. 2010:peds. 2008-3256.
33. Mwangi MN, Phiri KS, Abkari A, Gbané M, Bourdet-Sicard R, Braesco VA, et al. Iron for Africa—Report of an Expert Workshop. Multidisciplinary Digital Publishing Institute; 2017.