ORIGINAL ARTICLE

Prenatal anemia control and anemia in children aged 6–23 months in sub-Saharan Africa

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Abstract

It is unclear whether routine prenatal anemia control interventions can reduce anemia risk in young children. This study examines the associations between prenatal iron supplementation and/or deworming and anemia in children aged 6–23 months in sub-Saharan Africa (SSA). We analyzed data from Demographic and Health Surveys conducted between 2003 and 2014 in 25 SSA countries. The surveys collected data on prenatal iron supplementation and deworming and determined children's hemoglobin levels through blood testing. We assessed the associations between prenatal iron supplementation and/or deworming and anemia using multinomial logistic regression. The study included 31,815 mother–child pairs: 25.0%, 41.4%, and 4.8% of children had mild, moderate, and severe anemia, respectively. Compared with children whose mothers did not take iron and deworming drugs prenatally, the risk of moderate/severe anemia was reduced among children whose mothers took only iron supplements for ≥ 6 months (odds ratio [OR]: 0.58; 95% confidence interval [CI]: 0.45–0.76); only deworming drugs (OR: 0.73; 95% CI: 0.56–0.93); deworming drugs plus iron for < 6 months (OR: 0.79; 95% CI: 0.67–0.93); and deworming drugs plus iron for ≥ 6 months (OR: 0.77; 95% CI: 0.59–0.99). Prenatal use of only iron for < 6 months was not associated with moderate/severe anemia. Prenatal iron and/or deworming drugs had no effect on mild anemia. Prenatal anemia control interventions are associated with reduced risk of moderate/severe anemia but not with mild anemia in young children in SSA. Iron supplements should be taken for ≥ 6 months or with deworming drugs prenatally to reduce moderate/severe anemia risk in children.

KEYWORDS

anemia control, child nutrition, deworming, iron supplementation, low-income countries

1 | INTRODUCTION

Anemia is a persistent public health problem that affects about a third of the global population, mainly children and pregnant women (Kassebaum et al., 2014). Globally, about 43% of children younger than 5 years are anemic (Stevens et al., 2013). In sub-Saharan Africa (SSA), the prevalence of anemia in children ranges from 46% in southern Africa to 71% in central and west Africa, the highest of any World Health Organization (WHO) region (Stevens et al., 2013).

Anemia has multifactorial etiology: Iron deficiency is the leading cause, accounting for about 60% of anemia in children aged 1 month–4 years (Kassebaum et al., 2014). Other major causes include hookworm infestation, sickle cell disorders, thalassemias,

schistosomiasis, malaria, and micronutrient deficiency (Balarajan et al., 2011; Kassebaum et al., 2014).

Iron deficiency anemia in infants is associated with potentially irreversible diminished mental, psychomotor, and behavioral development (Akman et al., 2004; Pala et al., 2010; Lozoff et al., 1991; Lozoff et al., 2006). In a recent meta-analysis, iron supplementation among children did not improve their mental or psychomotor development, maybe due to an irreversible cognitive deficit in children that is intractable to iron supplementation (Pasricha et al., 2013).

Public health interventions to control anemia in developing countries have focused primarily on iron supplementation, and to some extent, control of soil-transmitted helminths. Among pregnant women in countries with at least 40% prevalence of anemia in pregnancy, WHO recommends a daily dose of iron plus folic acid

to prevent anemia and adverse birth outcomes (WHO, 2013). Daily iron supplementation for at least 6 months is sufficient to meet the physiological requirements for iron in pregnancy (WHO, 2007). In areas where the prevalence of any soil-transmitted helminth infection exceeds 20%, WHO recommends administration of deworming drugs to pregnant women in the second and third trimesters of pregnancy as a prophylaxis against infection (WHO, 2006). Consequently, these two interventions have become part of antenatal care in SSA. However, deworming during pregnancy is still controversial; a recent review found insufficient evidence to recommend it (Salam et al., 2015).

Anemia during pregnancy increases the risk of iron deficiency during infancy (Kilbride et al., 1999; Kilbride et al., 2000). However, it is unclear whether routine prenatal iron supplementation and/or deworming drugs can reduce the risk of anemia in young children. In a small-scale trial of the effects of prenatal iron supplementation, serum ferritin concentrations were significantly higher in infants born to women in the iron-supplemented group 3 months after delivery (Preziosi et al., 1997), suggesting that prenatal iron supplementation may have long-term effects on offspring iron status. Using nationally representative data from SSA countries, this study aimed to investigate whether routine prenatal iron supplementation, with or without folate, and/or deworming can reduce anemia risk in children aged 6–23 months.

2 | MATERIALS AND METHODS

2.1 | Data source and design

This study utilized data from most recent Demographic and Health Surveys (DHS) from SSA countries. The DHS program represents the largest effort to obtain health and demographic data from nationally representative household surveys in low-income and middle-income countries.

DHS collect data utilizing stratified multistage cluster sampling method. In the first stage, clusters (primary sampling units) are selected from a list of enumeration areas, using stratified random sampling, with regions constituting strata. The second stage involves systematically sampling households in selected clusters. All women aged 15–49 years who are present in the household on the night before the surveys are eligible for interview. Blood samples are collected from all the households or from a random subset of selected households based on considerations such as required sample size, financial costs, and logistics.

DHS use household and women's questionnaires to collect data relevant to women and children. The household questionnaire is used to collect data on characteristics of the household's dwelling unit and to record height, weight, and hemoglobin (Hb) measurements of women aged 15–49 years and children. The women's questionnaire is used to collect data from all women aged 15–49 years on various issues including socio-demographics, birth history, maternal and child health, and nutrition. Details about the DHS methodology and tools are available elsewhere (Rutstein and Rojas, 2006, The DHS Program, 1987–2016).

We included in this study all SSA countries with a severe public health problem of anemia in children—defined as anemia prevalence of >40% in preschool-aged children (WHO, 2008)—if their latest DHS were conducted after the year 2000, and the dataset contains information on Hb measurement, iron supplementation, and use of deworming drugs during pregnancy. Appendix 1 shows the list of included countries and the percentage of households selected for Hb measurement in each country. Appendix 2 shows the list of excluded countries, with reasons for exclusion. The study population for the present analysis is children aged 6–23 months and their mothers.

2.2 | Outcome variable

The outcome variable was anemia, adjusted for altitude and categorized as none (Hb ≥ 11.0 g/dl), mild (Hb 10–10.9 g/dl), moderate (Hb 7.0–9.9 g/dl), and severe (Hb <7.0 g/dl; Sharman, 2000; WHO, 2011). In regression analyses, the last two categories were combined because the proportion of children with severe anemia was small (4.8%). The DHS program tests for anemia in a standardized way across surveys (Sharman, 2000): Blood specimens are collected from children aged 6–59 months using a microcuvette from a drop of blood taken from a finger or heel prick (for undernourished/skinny children), and Hb analysis is carried out on-site using a battery-operated portable HemoCue® analyzer (HemoCue, Ängelholm, Sweden), a highly valid method when compared to standard laboratory methods (Nkrumah et al., 2011). General procedures for collecting blood samples are available elsewhere (ICF International, 2012).

2.3 | Exposure variable

Women with a live birth 5 years preceding the survey were asked whether, during the pregnancy of the most recent birth, they took iron tablets or syrup (with or without folic acid), the number of days they consumed the supplements, and whether they took drugs for intestinal worms. We used this information to define the exposure variable,

Key messages

- Prenatal anemia control through routine iron supplementation and deworming is associated with reduced risk of moderate/severe anemia but not with mild anemia in young children.
- Taking only iron supplements for less than 6 months during pregnancy does not reduce the risk of anemia in young children.
- Strengthening prenatal anemia control interventions can contribute towards reducing the risk of anemia in children in low-income countries.

TABLE 1 Characteristics of 31,815 children aged 6–23 months by prenatal anemia control intervention in 25 sub-Saharan African countries

Characteristics	Total n (%) ^a	Prenatal anemia control intervention (%)							Iron for unknown period ± deworming
		None	Only iron for:		Only deworming	Deworming:			
			<6 months	≥6 months		Plus iron <6 months	Plus iron ≥6 months		
Number of children	31,815	6,584	10,567	1,105	1,274	9,248	1,226	1,811	
Child's anemia status									
No anemia	7,558 (28.9)	33.1	23.7	24.8	34.7	28.0	24.5	27.4	
Mild anemia	8,087 (25.0)	23.9	25.3	25.0	29.1	25.3	27.2	24.5	
Moderate	14,498 (41.4)	38.3	44.8	45.7	32.6	42.8	44.8	44.0	
Severe anemia	1,672 (4.8)	4.7	6.2	4.5	3.6	3.9	3.5	4.0	
Child's age, M, mean (SE)	14.1 (0.1)	14.0 (0.1)	14.1 (0.1)	13.9 (0.2)	14.3 (0.2)	14.0 (0.1)	14.5 (0.2)	14.3 (0.2)	
Female sex	15,889 (50.0)	49.0	50.7	47.8	53.1	50.1	48.7	52.8	
Mother's years of education									
0	13,948 (46.8)	60.5	45.1	37.2	29.8	34.1	25.6	47.9	
1–7	11,751 (36.2)	31.2	37.2	28.5	46.7	42.2	33.9	27.7	
8–11	4,873 (13.2)	7.0	14.7	22.6	17.7	17.4	27.1	16.9	
≥12	1,235 (3.9)	1.3	3.0	11.7	5.8	6.3	13.4	7.5	
Missing data	8 (0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Mother's age, years, mean (SE)	27.2 (0.1)	27.2 (0.1)	27.0 (0.1)	27.3 (0.3)	27.1 (0.3)	27.3 (0.1)	27.2 (0.3)	27.5 (0.3)	
Primiparous	6,582 (19.6)	17.8	20.8	25.2	21.0	19.7	24.3	22.0	
Cesarean section delivery									
No	30,463 (96.3)	98.3	96.0	91.2	96.1	95.0	92.1	93.4	
Yes	1,294 (3.6)	1.7	3.8	8.6	3.7	4.9	7.8	6.5	
Missing data	58 (0.0)	0.0	0.2	0.2	0.1	0.1	0.2	0.1	
Wealth index quintile									
1	4,387 (20.0)	30.4	14.9	3.9	22.7	13.9	2.7	7.8	
2	4,686 (20.0)	25.2	17.9	4.2	26.2	17.2	3.8	10.3	
3	5,780 (20.0)	21.6	20.3	11.3	17.9	20.0	7.4	15.8	
4	7,869 (20.0)	14.7	24.7	19.5	15.7	23.2	18.1	24.6	
5	9,093 (20.0)	8.1	22.2	61.2	17.4	25.7	68.0	41.5	
Rural residence	23,196 (77.5)	87.8	78.1	51.8	74.8	69.3	40.1	60.1	
Cooking fuel ^b									
Clean fuel	2,133 (3.9)	1.5	4.3	21.2	1.8	3.7	21.8	9.5	
Mixed fuel	4,592 (13.2)	5.6	13.2	16.8	15.8	21.8	27.9	20.4	
Biomass fuel	25,085 (82.9)	92.9	82.5	62.0	82.4	74.5	50.3	70.1	
Missing data	5 (0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Year of interview									
Before 2009	4,068 (31.5)	61.6	19.8	14.1	20.8	7.5	12.6	10.1	

(Continues)

TABLE 1 (Continued)

Characteristics	Total n (%) ^a	Prenatal anemia control intervention (%)							Iron for unknown period ± deworming
		None	Only iron for:		Only deworming	Deworming:		Plus iron ≥6 months	
			<6 months	≥6 months		Plus iron <6 months	Plus iron ≥6 months		
2009–2010	7,393 (13.9)	7.4	23.1	24.9	9.7	13.2	12.0	12.5	
2011–2012	13,436 (32.9)	17.5	42.5	53.5	16.1	42.6	60.8	49.4	
2013–2014	6,918 (21.7)	13.5	14.6	7.4	53.5	36.8	14.7	28.0	
Mother's body mass index									
18.5–25.0 kg/m ²	22,314 (71.4)	72.6	73.7	58.3	70.3	69.7	62.3	68.0	
<18.5 kg/m ²	4,185 (15.6)	20.7	12.9	10.0	17.7	12.6	6.2	9.6	
>25.0 kg/m ²	5,026 (12.3)	6.3	12.7	31.0	11.4	16.8	30.5	21.5	
Missing/invalid data	290 (0.6)	0.4	0.7	0.8	0.6	0.9	1.1	0.9	
Child wasted ^d									
No	25,041 (80.8)	79.9	82.0	84.3	78.7	80.6	87.0	79.8	
Yes	3,579 (11.6)	13.9	10.8	9.0	10.0	10.5	6.1	9.1	
Missing/invalid data ^e	3,195 (7.6)	6.2	7.3	6.7	11.3	8.9	6.9	11.1	
Consumed vitamin A/iron rich foods past 24 hr ^f									
No	14,035 (48.5)	60.8	46.0	40.5	35.4	37.7	37.3	43.4	
Yes	17,702 (51.4)	39.2	53.8	59.5	64.5	62.2	62.3	56.4	
Missing data	78 (0.1)	0.1	0.2	0.0	0.1	0.1	0.4	0.2	
Child had pneumonia past 2 weeks ^g	2,118 (7.8)	8.5	7.6	4.3	7.1	8.0	5.5	5.4	
Child had diarrhea past 2 weeks ^h									
No	23,744 (73.5)	75.3	73.1	73.8	69.2	71.2	74.0	78.8	
Yes	8,059 (26.5)	24.7	26.9	26.2	30.7	28.7	25.7	21.2	
Missing data	12 (0.0)	0.0	0.0	0.0	0.0	0.0	0.3	0.0	
Child had fever past 2 weeks									
No	22,981 (71.7)	75.3	70.2	77.5	70.5	68.0	70.7	70.1	
Yes	8,800 (28.2)	24.6	29.7	22.5	29.5	31.9	29.2	29.8	
Missing data	24 (0.1)	0.2	0.2	0.0	0.1	0.1	0.1	0.1	

^aAll the frequencies are unweighted, but the percentages are weighted.^bBiomass fuels are as follows: wood, animal dung, or crop residues; mixed fuels are as follows: mix of biomass fuels and cleaner fuels, or coal/coke/lignite/charcoal; and cleaner fuels are as follows: kerosene, petroleum gas, biogas, or electricity.^cBMI <12.0 or >60.0.^dWasting is a sign of acute malnutrition. A wasted child was one with weight-for-height Z-score of <2 standard deviation units below the median of the World Health Organization's international reference population.^eWeight for height Z-score <-4 or >+6 standard deviation units with reference to the median of the World Health Organization's international reference population.^fVitamin A/iron rich foods included meat (and organ meat), fish, poultry, eggs, pumpkin, red or yellow yams or squash, carrots, red sweet potatoes, and dark-green leafy vegetables.^gPneumonia is defined as having symptoms of acute respiratory infection characterized by cough accompanied by short, rapid breathing and/or by difficult breathing, which were chest related. The symptoms were reported by the child's caretaker.^hThree or more loose or liquid stools with or without blood loss per day as reported by the child's caretaker.

referred to as prenatal anemia control intervention, as follows: none (no iron supplements and no deworming drugs); only iron supplements for <6 months; only iron supplements for ≥6 months; only deworming; deworming plus use of iron supplements for <6 months; and deworming plus use of iron supplements for ≥6 months. Due to missing data on the number of days iron was consumed, we created another category of iron for unknown period ± deworming. Women who did not take iron supplements and deworming drugs constituted the reference group in all comparisons.

2.4 | Potential confounders

These included child, maternal, household, and contextual factors. Child's factors included age, sex, wasted, consumed iron/vitamin A rich foods in past 24 hr, and had pneumonia, diarrhea, and fever in the preceding 2 weeks. Maternal factors included mother's age at childbirth, years of education, parity, delivered by cesarean section, and body mass index (weight in kilograms per height in square meter). Household factors included wealth index quintile and type of cooking fuel. Wealth index quintiles were derived through factor analysis of ownership of household assets, access to public utilities, and type of housing material (Rutstein and Rojas, 2006). The first of the obtained factor scores was used to represent the wealth index (Rutstein and Rojas, 2006). Contextual factors included survey year, residence (urban/rural), and country. Details of the definitions of potential confounders are available in the footnotes of Table 1.

2.5 | Statistical methods

We created a dataset of eligible children by merging DHS datasets and excluding children aged <6 months or ≥24 months. Because the analysis involved combining data from different surveys, we first de-normalized weights in each dataset by dividing the individual standard weight by the survey sampling fraction. Throughout the analyses, we used survey analysis functions to account for the primary sampling unit (cluster), strata, and sample weights. Accounting for clustering in the sample avoids underestimation of variability in the estimates by adjusting standard errors and confidence intervals (CIs), and weighting the data ensures representativeness.

We tabulated the exposure variable against the outcome and the potential confounding variables. All the presented frequencies are unweighted, but the percentages are weighted to account for the study design. We used multiple imputation using chained equations to impute missing covariates' data (StataCorp, 2013). We created 10 imputed datasets using an imputation model that included all the covariates listed previously plus mother's anemia status, births in the past 5 years, place of delivery, stunting (child), strata, and country. We calculated unadjusted and adjusted odds ratios (ORs) and 95% CIs for the association between the exposure and the outcome using multinomial logistic regression. All the effect estimates and standard errors from imputed datasets were automatically combined using Rubin's rules (Rubin, 2008). We considered variables that are associated with anemia in children based on previous studies (Kyu et al., 2010; Mishra and Retherford, 2007; Li et al., 2015) or those associated with both the exposure and the outcome, at $p < .2$ threshold, in our unadjusted results, to be potential confounders. Because the variable "country" met the later criterion, the multivariate model was a fixed-effects model that accounted for between-country differences. We considered child's birth weight, stunting, and mother's anemia status at the time of the survey to be on the causal pathway between the exposure and the outcome and did not adjust for these variables. Mother's and child's age and wealth index quintiles were entered in the model as continuous variables. Because anemia risk in children increases with child's age (Crawley, 2004), we assessed for interaction between prenatal anemia control and child's age (6–13 months and 14–23 months). We present two-sided p values of ORs from Wald's tests; p values of ≤.05 are considered to be statistically significant. All analyses were performed in Stata/MP version 13.1 (StataCorp, College Station, USA).

2.6 | Ethics

During the surveys, informed consent was obtained for oral interviews and for biomarker measurements. The results of Hb measurement of children were given to their parents, both verbally and in writing, and parents of children with Hb <7 g/dl were instructed to take their children to health facilities for follow-up care. This study was exempted from ethical review by the ethical review board of Kyoto University

FIGURE 1 Flowchart for the selection of children aged 6–23 months from demographic and health surveys of 25 sub-Saharan African countries. Hb, hemoglobin

Graduate School of Medicine because it is based on de-identified open-source datasets.

3 | RESULTS

3.1 | Characteristics of the study subjects

The final study subjects comprised 31,815 mother–child pairs from 25 countries (Figure 1). About 32% of mothers took neither iron

supplements nor deworming tablets prenatally, and only 2.0% took both iron supplements for ≥ 6 months and deworming tablets. Overall, 71.1% of children had any anemia; 25% were mildly anemic; 41.4% were moderately anemic; and 4.8% were severely anemic (Table 1), and this varied by prenatal anemia control intervention.

Half of the children were male, and 47% had mothers with no formal education. The mean age of the mothers was 27 years, and the proportion in the highest wealth group was lowest (8.1%) in those without any prenatal anemia control intervention and highest (68.0%) in those who took both iron supplements for ≥ 6 months and

TABLE 2 Adjusted effects of prenatal anemia control interventions and other risk factors on the risks of mild anemia and moderate/severe anemia in 31,815 children aged 6–23 months

	Mild anemia		Moderate/severe anemia	
	Adjusted OR (95% CI) ^a	p Value	Adjusted OR (95% CI) ^a	p Value
Prenatal anemia control intervention				
None	1		1	
Only iron supplements for <6 months	1.13 (0.97–1.32)	.13	0.98 (0.85–1.15)	.84
Only iron supplements for ≥ 6 months	0.83 (0.62–1.10)	.19	0.58 (0.45–0.76)	<.001
Only deworming	1.04 (0.78–1.38)	.80	0.73 (0.56–0.93)	.013
Deworming plus iron supplements <6 months	0.92 (0.78–1.08)	.32	0.79 (0.67–0.93)	.005
Deworming plus iron supplements ≥ 6 months	0.97 (0.74–1.27)	.81	0.77 (0.59–0.99)	.039
Iron for unknown period $\pm$ deworming	0.86 (0.65–1.15)	.32	0.75 (0.58–0.96)	.021
Child's age	0.97 (0.96–0.98)	<.001	0.96 (0.95–0.97)	<.001
Female child	0.99 (0.88–1.11)	.84	0.80 (0.71–0.90)	<.001
Mother's age at childbirth	1.00 (0.99–1.00)	.34	0.99 (0.98–0.99)	.009
Primiparous	1.01 (0.85–1.21)	.88	0.96 (0.81–1.12)	.58
Delivered by cesarean section	0.97 (0.72–1.30)	.82	1.00 (0.79–1.26)	1.00
Mother's years of education				
0	1		1	
1–7	0.95 (0.80–1.12)	.52	0.90 (0.78–1.03)	.13
8–11	0.95 (0.77–1.17)	.61	0.81 (0.67–0.97)	.022
≥ 12	0.66 (0.50–0.87)	.004	0.60 (0.45–0.79)	<.001
Wealth index quintile	0.97 (0.91–1.03)	.30	0.91 (0.86–0.96)	.001
Rural residence	0.98 (0.83–1.15)	.79	0.98 (0.81–1.19)	.84
Cooking fuel				
Clean fuel	1		1	
Mixed fuel	1.28 (1.00–1.64)	.05	1.24 (0.97–1.59)	.08
Biomass fuel	1.11 (0.87–1.41)	.39	1.25 (0.97–1.61)	.08
Year of survey				
Before 2009	1		1	
2009–2010	1.35 (0.88–2.05)	.17	1.17 (0.78–1.74)	.45
2011–2012	1.40 (0.87–2.23)	.16	0.99 (0.63–1.54)	.96
2013–2014	1.32 (0.68–2.57)	.41	0.74 (0.39–1.38)	.34
Mother's body mass index				
18.5–25.0 kg/m ²	1		1	
<18.5 kg/m ²	0.99 (0.84–1.17)	.92	0.96 (0.81–1.14)	.62
>25.0 kg/m ²	0.90 (0.76–1.06)	.21	0.79 (0.69–0.91)	.001
Child wasted	1.08 (0.89–1.31)	.43	1.23 (1.02–1.46)	.033
Consumed vitamin A/iron rich food past 24 hr	1.02 (0.91–1.15)	.72	0.96 (0.85–1.07)	.44
Child had pneumonia past 2 weeks	0.69 (0.55–0.86)	.001	0.80 (0.66–0.98)	.029
Child had diarrhea past 2 weeks	0.98 (0.85–1.13)	.77	0.95 (0.84–1.08)	.44
Child had fever past 2 weeks	1.21 (1.05–1.41)	.010	1.48 (1.29–1.69)	<.001

^aAdjusted for all the variables in the table and country. OR, odds ratio; CI, confidence interval.

deworming tablets. About 76% of children were from rural areas; 82.9% were from households that use biomass for cooking; 12% were wasted; and 51.4% had consumed iron and/or vitamin A rich foods a night before the survey. In the past 2 weeks, 7.8% of children had suffered from pneumonia; 26.6% had suffered from diarrhea; and 28.2% had had fever. About 12% of the mothers had a BMI of $>25 \text{ kg/m}^2$.

3.2 | Effects of prenatal anemia control interventions

In unadjusted analysis, compared with children whose mothers did not take iron and deworming drugs prenatally, the risk of mild anemia was significantly higher in children whose mothers took only iron supplements for <6 months; only iron supplements for ≥ 6 months; deworming plus iron supplements for <6 months; and deworming plus iron supplements for ≥ 6 months (Appendix 3). Similar associations were observed for moderate/severe anemia. After adjusting for confounding factors, none of the prenatal anemia control interventions was significantly associated with mild anemia in children (Table 2). On the contrary, the risk of moderate/severe anemia in children was reduced with prenatal use of only iron for ≥ 6 months (OR: 0.58; 95% CI: 0.45–0.76), only deworming (OR: 0.73; 95% CI: 0.56–0.93), deworming plus iron supplements for <6 months (OR: 0.79; 95% CI: 0.67–0.93), and deworming plus iron supplements for ≥ 6 months (OR: 0.77; 95% CI: 0.59–0.99). Child's age, pneumonia, and fever, and mother's education were associated with both mild and

moderate/severe anemia, while child's sex, mother's age at childbirth, mother's body mass index, and wealth index quintile were associated with only moderate/severe anemia. There was significant interaction between prenatal anemia control and anemia in children ($p < .001$), and age stratum-specific effects are presented. Prenatal anemia control interventions tended to have non-significant protective effects against mild anemia mainly among older children (Figure 2). Prenatal anemia control was generally protective of moderate/severe anemia in children, but some significant effects were observed only in the older children (Figure 3).

4 | DISCUSSION

In this study, using nationally representative data of 31,815 mother-child pairs from 25 SSA countries, 25.0% and 46.1% of children had mild and moderate/severe anemia, underscoring the continuing burden of anemia in this setting. Prenatal supplementation of only iron for at least 6 months and deworming with or without iron supplements for any duration were associated with reduced risk of moderate/severe anemia. Use of only iron supplements for at least 6 months had the strongest association with moderate/severe anemia, whereas use of only iron for less than 6 months was not associated with anemia. Prenatal anemia control had no significant association with mild anemia in children.

FIGURE 2 Adjusted effects of prenatal anemia control interventions on mild anemia in children, stratified by child's age. *Adjusted for child's age and sex; mother's age; parity; mode of delivery; education; body mass index; household's wealth index quintile; place of residence; type of cooking fuel; year of survey; child wasted; child consumed vitamin A/iron rich food in past 24 hr; child had pneumonia, diarrhea, and fever in the past 2 weeks; and country. OR, odds ratio; CI, confidence interval

FIGURE 3 Adjusted effects of prenatal anemia control interventions on moderate to severe anemia in children, stratified by child's age. *Adjusted for child's age and sex; mother's age; parity; mode of delivery; education; body mass index; household's wealth index quintile; place of residence; type of cooking fuel; year of survey; child wasted; child consumed vitamin A/iron rich food in past 24 hr; child had pneumonia, diarrhea, and fever in the past 2 weeks; and country. OR, odds ratio; CI, confidence interval

The strength of this study is in the use of a large sample of children from nationally representative surveys in which Hb testing was performed in a standard way (Sharman, 2000); hence, the findings are generalizable to populations in SSA. The sample size allowed us to look at the associations between anemia in children and different combinations of prenatal anemia control interventions.

Although we adjusted for a large number of potential confounders, data on the anemia status of mothers before or during pregnancy were not available. It is possible that severely anemic pregnant mothers were more likely to have taken iron and/or deworming tablets as part of routine antenatal care or anemia treatment. Thus, this study may have underestimated the effects of prenatal anemia control interventions on anemia in children.

In the DHS, women were asked to recall the number of days they consumed iron tablets or syrup during the last pregnancy, which may result in recall bias. Given that anemia testing in the DHS was done after the interview, however, the recall problem is more likely to be non-differential, and the direction of bias would be towards the null. The recall problem might have also affected the precision in measurement of the number of days iron was consumed: The number of days tended to cluster at 30 days intervals, suggesting that respondents were rounding off the number of days to the nearest month. This is also likely to have happened non-differentially. In the DHS, women were aided to recall prenatal iron consumption by showing them samples of iron tablets/syrup. This was not done when inquiring about

prenatal deworming. Data on pneumonia, cough, and fever were based on a 2-week recall period and are also subject to recall bias, though to a lesser extent. Information on the validity of responses based on recall in DHS is limited; nevertheless, studies conducted elsewhere show that women are good at recalling events related to pregnancy and child health (McCormick and Brooks-Gunn, 1999; Yawn et al., 1998). We tried to minimize the problem of recall bias in our analyses by focusing on the most recent birth, which took place in the past 2 years preceding the survey. Another limitation of this study is that it is based on data collected through cross-sectional surveys; hence, it is subject to the limitations inherent in this study design (Mann, 2003). Nevertheless, given that the outcome preceded the exposure, the problem of reverse causality is precluded.

During pregnancy, iron is actively transported across the placenta from maternal to fetal circulation (McArdle et al., 2008). Iron endowed from maternal circulation is the main source of iron for infants during the first months of infancy (Chaparro, 2008), and possession of sufficient iron stores at birth is important in ensuring steady supply of iron to the rapidly growing infant tissues. Longitudinal studies have shown that iron deficiency during pregnancy can affect fetal iron deposit enough to have long-term effects (De Pee et al., 2002; Preziosi et al., 1997; Kilbride et al., 2000; Colomer et al., 1990). Although most of these studies (Kilbride et al., 2000; Preziosi et al., 1997; Colomer et al., 1990) are small, consistent with our findings, they imply that prenatal anemia control is an important strategy

for preventing anemia in infants and in toddlers (Scholl, 2011). Our results further show that prenatal use of iron for a suboptimal duration may not be beneficial to young children probably because iron supplementation for less than 6 months is insufficient to meet the physiological requirements for iron in pregnancy (WHO, 2007). Consistent with our findings, a study that looked at the association between use of biomass for cooking and anemia in children, and included prenatal iron use as a covariate, reported a small reduction in the risk of moderate/severe anemia with each day of iron supplementation (relative risk ratio: 0.98; 95% CI: 0.97–0.99), but no effect on mild anemia (Kyu et al., 2010). However, similar studies did not find an association between prenatal use of iron supplements and anemia in children (Mishra and Retherford, 2007; Machisa et al., 2013). Our study focused on children aged 6–23 months and explored the effect of iron supplementation for different durations, which may partly explain the discrepancies.

Based on WHO recommendations, prenatal iron supplementation for more than 6 months plus deworming can be considered to be the optimal way to control anemia in pregnancy and in new-born children in high-prevalence countries. We therefore expected deworming plus iron supplements for ≥ 6 months to have a stronger or a similar protective effect against moderate/severe anemia compared with only iron supplements for ≥ 6 months, and deworming plus iron for any duration to have a stronger effect than only deworming. Given that the point estimates in our study do not follow this pattern, confounding remains a possibility. Nonetheless, in keeping with results from a systematic review (Smith and Brooker, 2010), our study did not find an additional benefit of deworming combined with iron supplements in reducing anemia risk in children.

Prenatal anemia control interventions were not associated with mild anemia in children in the present study. This could be because the cut-off values for mild anemia (i.e., Hb 10–10.9 g/dl) narrowly distinguish it from no anemia, thus increasing the chance of non-differential misclassification of the outcome resulting into biasing the effect estimates towards the null. On the contrary, there is a clearer distinction between no anemia and moderate/severe anemia, minimizing the risk of outcome misclassification.

In the stratified analyses, the point estimates are consistent with prenatal anemia control being protective of moderate/severe anemia especially in older children. Some of the effects are however not significant probably because of the reduced sample size. For mild anemia, the point estimates, though not significant, are consistent with a protective effect among older children only. Hb levels in young children rapidly decline in the first 3 months reaching nadir at around 1 year (Crawley, 2004). Thus, infants who start off with lower iron stores are likely to develop anemia as they advance in age, unless their iron intake is sufficient.

5 | CONCLUSIONS

Routine prenatal anemia control interventions are associated with reduced risk of moderate/severe anemia in young children in SSA. However, iron supplements should be taken for at least 6 months or in addition to deworming drugs prenatally for the effect to be realized.

Our findings highlight the need to strengthen routine prenatal anemia control interventions in SSA through strengthening health systems to improve the quality of prenatal care, and providing nutrition health education to women of reproductive age. There is also need to improve compliance with iron supplementation as this may be a problem (Gebremedhin et al., 2014; Seck and Jackson, 2008), and to promote initiation of iron supplementation as early as possible during pregnancy to maximize the chance of taking the supplements for at least 6 months. Further research on the relationship between prenatal anemia control interventions and anemia in children through well designed cohort studies is needed.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interests.

CONTRIBUTIONS

CW and ST designed the study. CW acquired and analyzed data under supervision of STCW drafted the initial manuscript. All authors participated in interpreting the data and in critically revising the manuscript for important intellectual content. All authors read and approved the final manuscript.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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