

# Dietary Factors Moderate the Relation between Groundwater Iron and Anemia in Women and Children in Rural Bangladesh

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## ABSTRACT

**Background:** Anemia affects ~1.6 billion people worldwide, often owing to iron deficiency. In Bangladesh, high levels of anemia have been observed alongside little iron deficiency. Elevated concentrations of groundwater iron could constitute a significant source of dietary iron.

**Objective:** We aimed to quantify the effect of groundwater iron on anemia in nonpregnant women and young children in Bangladesh, taking into account dietary factors that may affect iron absorption.

**Methods:** We analyzed data on 1871 nonpregnant women and 987 children (6–37 mo) from the 2015 baseline survey of the Food and Agricultural Approaches to Reducing Malnutrition cluster-randomized trial in Sylhet, Bangladesh. We used logistic regression with robust standard errors to assess effects of self-reported groundwater iron, dietary intake, and sociodemographic characteristics on anemia, considering interactions between groundwater iron and dietary factors.

**Results:** Groundwater iron presence was associated with less anemia in women (OR: 0.74; 95% CI: 0.60, 0.90) and children (OR: 0.58; 95% CI: 0.44, 0.76). This effect was modified by dietary factors. In women, the effect of groundwater iron on anemia was stronger if no vitamin C-rich or heme-iron foods were consumed, and there was a clear dose–response relation. In children, intake of vitamin C-rich foods strengthened the effect of groundwater iron on anemia, and there was no evidence for interaction by intake of iron-rich foods.

**Conclusions:** Heme-iron and vitamin C consumption reduced the effect of groundwater iron on anemia among women but not children in Bangladesh, which may be due to higher levels of iron deficiency and lower levels of iron intake among children. Vitamin C consumption appears to enhance iron absorption from groundwater in children and they may thus benefit from consuming more vitamin C-rich fruits and vegetables. Even among women and children consuming heme-iron or vitamin C-rich foods and groundwater iron, anemia prevalence remained elevated, pointing to additional causes of anemia beyond iron deficiency. This trial was registered at [clinicaltrials.gov](https://clinicaltrials.gov) as NCT02505711. *Curr Dev Nutr* 2019;3:nzz093.

## Introduction

Anemia, defined as a hemoglobin (Hb) concentration insufficient to meet physiological needs, reduces the body's ability to transport oxygen and can result in reduced cognitive function and fatigue (1–4). Anemia among pregnant women can lead to poor maternal and child health outcomes including reduced infant growth, impaired cognitive development, increased risk of maternal morbidities, and death (5–7). Iron deficiency can also lead to impaired cognitive development before anemia is apparent (8). Anemia is estimated to affect 29% of nonpregnant women (496 million) and 43% of children <5 y of age (273 million) worldwide, with the largest number



**Keywords:** anemia, iron, vitamin C, maternal and child nutrition, groundwater, diet, tube well, Bangladesh

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Supplemental File 1, Supplemental Tables 1–3, and Supplemental Figures 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/cdn/>.

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Abbreviations used: FAARM, Food and Agricultural Approaches to Reducing Malnutrition; Hb, hemoglobin; HFP, Homestead Food Production; IDA, iron deficiency anemia; IFA, iron and folic acid.

of affected women and children living in South Asia (9). The WHO estimates that 50% of anemia cases are due to iron deficiency when anemia prevalence is >20% (2). This assumption has recently been called into question by studies from Bangladesh and other countries, which have shown little or no iron deficiency in populations with elevated anemia prevalence in women (26–57%) and preschool-aged children (33%) (3, 10, 11). In Bangladesh, nationally representative dietary intake data have furthermore found vastly inadequate iron intakes, in spite of the low levels of iron deficiency. This may point to a different source of iron intake, not captured through dietary assessment (3).

Iron content in groundwater is a well-established phenomenon and is largely considered a nuisance at higher concentrations (>0.3 mg/L) owing to its unpleasant color and taste (12). Recent studies have found associations between consumption of groundwater with high iron content and both iron status and Hb concentrations (13, 14). A study in northwestern Bangladesh found a 6% increase in serum ferritin for each 10-mg increase in daily groundwater iron intake among women (14). At the national level, higher ferritin concentrations in both women and children were found in geographic regions identified as having high groundwater iron (13). However, a 2015 follow-up study found substantial variability of groundwater iron within high and low groundwater iron areas. Low groundwater iron (<1 mg/L) was found in 75% of samples from “low groundwater iron” areas, whereas in areas geographically classified as having high groundwater iron, 46% had low iron (15). Furthermore, within high groundwater iron areas, households may not consume groundwater as their primary water source or may use treatment practices, such as filtering, which would greatly reduce iron intake from water. Comprehensive water testing is often impractical to implement as part of routine dietary assessments. However, owing to the distinct flavor and color profile of water with high amounts of iron, Merrill et al. (14) found that women were able to reliably report the amount of iron in their drinking water on a 4-point scale, which was highly correlated with the measured amount of iron consumed through groundwater.

Previous studies examining the effect of dietary iron on anemia and iron status while adjusting for groundwater iron have reported mixed results, likely due to varying sample sizes, geographic regions, and groundwater classifications (10, 13, 15). No studies to date have examined potential interactions between groundwater iron and dietary factors. Because water is often consumed together with food (16), it is possible that certain dietary intakes (e.g., vitamin C, phytates, tannins) affect absorption of groundwater iron. In particular, vitamin C, a well-known enhancer of nonheme-iron absorption, is a potential candidate because it increases the bioavailability of iron by forming iron chelate complexes, when consumed simultaneously with iron sources (17–19). The objective of this study was to assess the effect of perceived groundwater iron on anemia in a large sample of nonpregnant women and young children, taking into account potential interactions with dietary factors.

## Methods

### Study population

Data analyzed for this study are from the baseline survey of the Food and Agricultural Approaches for Reducing Malnutrition (FAARM)

cluster-randomized controlled trial (NCT02505711) in rural Habiganj District, Sylhet Division, Bangladesh. The aim of the FAARM trial is to evaluate the impact of a Homestead Food Production (HFP) program implemented by Helen Keller International on undernutrition in women and young children. The HFP program works through women farmer groups who receive training on gardening and poultry rearing, as well as nutrition and hygiene counseling. Women were included in the study if they reported being 30 y of age or younger at enumeration, were married to a husband who stayed overnight at the household at least once in the year before interview, had access to  $\geq 40$  square meters of land, and were interested to participate in a gardening project. The minimum settlement size was 10 eligible women and the minimum distance between settlements was 400 m. Further information about the design and baseline data collection is reported in our study protocol (20).

### Data collection

The FAARM baseline survey, conducted from March to May 2015, included questions on age, sociodemographic characteristics, pregnancy status, dietary intake, groundwater iron perception, as well as anthropometric measurements, and blood collection. Enrolled women answered questions about their youngest biological child (0–37 mo). Wealth quintiles were calculated using principal component analysis of a household asset list adapted from that used in the Bangladesh Demographic and Health Survey (21). Women’s education was measured as number of school years completed. Groundwater iron of the domestic tube well used as the primary drinking or cooking source was assessed by asking each woman, “How much iron do you think is in your groundwater?” using a 4-point scale (none, a little, a medium amount, a lot), a question validated by Merrill et al. (16) in rural northwestern Bangladesh and recently by Rahman et al. (22). We also validated this question in a subset of households ( $n = 896$ ) in 2017 (**Supplemental File 1**). Mean water iron content increased continuously over the 4 perception categories: none: 2.7 mg/L; a little: 4.9 mg/L; a medium amount: 6.6 mg/L; a lot: 7.8 mg/L (**Supplemental Figure 1**). The few women who reported that they did not know how much iron was in their water ( $n = 9$ ) were reclassified into the “no iron” group.

Dietary diversity (of the woman and then her child) was assessed first by open recall of any foods or beverages consumed in the previous 24 h. Follow-up questions were then asked for any food groups not mentioned. We collected information on 21 food groups (23, 24), which were then collapsed to 10 food groups to assess dietary diversity in women (i.e., starchy staples; pulses; nuts and seeds; dairy; meat, poultry, and fish; eggs; dark green leafy vegetables; vitamin A–rich fruits and vegetables; other vegetables; and other fruits) (**Supplemental Table 1**). If a woman consumed <15 g (~1 spoonful) of a food group during the entire 24-h period, this group was not considered consumed, in accordance with the updated minimum dietary diversity guidelines (25). Women were considered to have an adequately diverse diet if they consumed  $\geq 5$  out of 10 food groups. Children met minimum dietary diversity by consuming  $\geq 4$  out of 7 food groups (i.e., starchy staples; legumes and nuts; dairy; meat, poultry, and fish; eggs; vitamin A–rich fruits and vegetables; and other fruits and vegetables), in line with the WHO’s Infant and Young Child Feeding guidelines (26). Food groups collected and used for dietary diversity calculations are listed in Supplemental Table 1.

Teams of data collectors measured Hb concentrations with the Hemocue 201+ with standard methods, using capillary blood by finger prick from women and from children  $\geq 6$  mo of age. Both women's and children's weights were measured using the SECA 874 scale. Women's heights were assessed with the SECA 217 stadiometer and children's lengths with a SECA 416 infantometer. BMI (in  $\text{kg}/\text{m}^2$ ) was then calculated for women as well as stunting and wasting for children (i.e., length-for-age and weight-for-length below  $-2$  SDs of the reference population) (27, 28). Further details are published in our study protocol (20).

From September 2015, all households enrolled in the FAARM trial were targeted for visits every 2 mo as part of a surveillance system. In the first 2 rounds of data collection, we asked women about supplement consumption in the past year. For those who had consumed iron supplements, we asked in which months any iron supplements were consumed. Women who reported taking any iron supplements during the month of Hb measurement or up to 3 mo before were classified as having consumed iron supplements for the purpose of this analysis.

### Inclusion and exclusion criteria

A total of 2573 women completed all baseline survey components. Women who were pregnant, did not have an Hb measurement, did not use a tube well as their main drinking water source, or regularly filtered their water were excluded from the analysis. In cases where multiple enrolled women were surveyed from the same household, 1 woman per household was randomly selected and the others were excluded. In total, 1871 women were included in this analysis (Figure 1).

All baseline survey components were completed for 1532 children. Children  $< 6$  mo of age, without Hb measurements, who were exclusively breastfed, whose mothers did not know about all foods consumed by the child, whose households did not use tube well water as a primary drinking source, or whose households regularly filtered water were excluded. When multiple children per household were surveyed, 1 child at random was selected for inclusion to avoid clustering at the household level. We included 987 children in our analysis (Figure 1).

### Variables

Anemia was the outcome variable for both women and children. In line with WHO recommendations, nonpregnant women with an Hb value  $< 12.0$  g/dL were considered anemic (mildly: 11.0–11.9 g/dL; moderately: 8.0–10.9 g/dL; severely:  $< 8.0$  g/dL), whereas for children, 11.0 g/dL was used as a cutoff for anemia (mild: 10.0–10.9 g/dL; moderate: 7.0–9.9 g/dL; severe:  $< 7.0$  g/dL) (4). Owing to the low elevation of the Bangladesh study site, adjustments for altitude were not required.

In addition to minimum dietary diversity, we assessed specific food groups which were iron-rich or contained vitamin C, which enhances iron absorption (29), both as individual food groups and as combined groups. Combined groups for women included animal-source heme-iron foods (meat, poultry, organ meat, and fish), nonheme-iron plant-based foods (dark green leafy vegetables and legumes), and vitamin C-rich foods (vitamin C-rich fruits or vegetables). Vitamin C-rich foods were defined as those containing  $> 9$  mg vitamin C/100 g serving (24). For children only, we also included consumption of any iron-fortified foods or micronutrient powders (which typically contain

iron) in the heme-iron food group, in line with the WHO definition of “iron-rich” foods for infant and young child feeding (26). Children who consumed micronutrient powders in the last 24 h were also considered as having consumed vitamin C for the analysis. In our sample, 21 children (2%) consumed iron-fortified products and 6 children (0.6%) consumed micronutrient powders in the last 24 h.

Besides adjusting for potential confounders of the relation between groundwater iron and anemia, we also considered confounders of the relation between diet and anemia, which include sociodemographic characteristics (30). Among women, we included household wealth, women's educational attainment, age, pregnancy history of the previous 3 y, and minimum dietary diversity. For children, we included child age, household wealth, mother's educational attainment, and minimum dietary diversity. Because the consumption of the studied food groups and overall dietary diversity are positively correlated, we also adjusted for minimum dietary diversity to ensure we examined the effect of the specific food group itself.

### Statistical analysis

We described outcome, exposure, and confounder variables as well as further sociodemographic characteristics and dietary intake using means  $\pm$  SDs or proportions. Population attributable fractions, using the Stata command *punaf*, were calculated to estimate the change in anemia prevalence if there was no (reported) groundwater iron, using final models with the vitamin C-by-groundwater iron interaction for both women and children. We used logistic regression with robust SEs to examine determinants of anemia in women and children. Multiplicative interactions between groundwater iron consumption and iron-rich or vitamin C-rich food intake in the past 24 h were assessed in separate models. To aid in interpretation, we also graphed each interaction using marginal standardization (Stata commands: *margins* and *marginsplot*), which calculates predicted probabilities of anemia from the final logistic regression model (31).

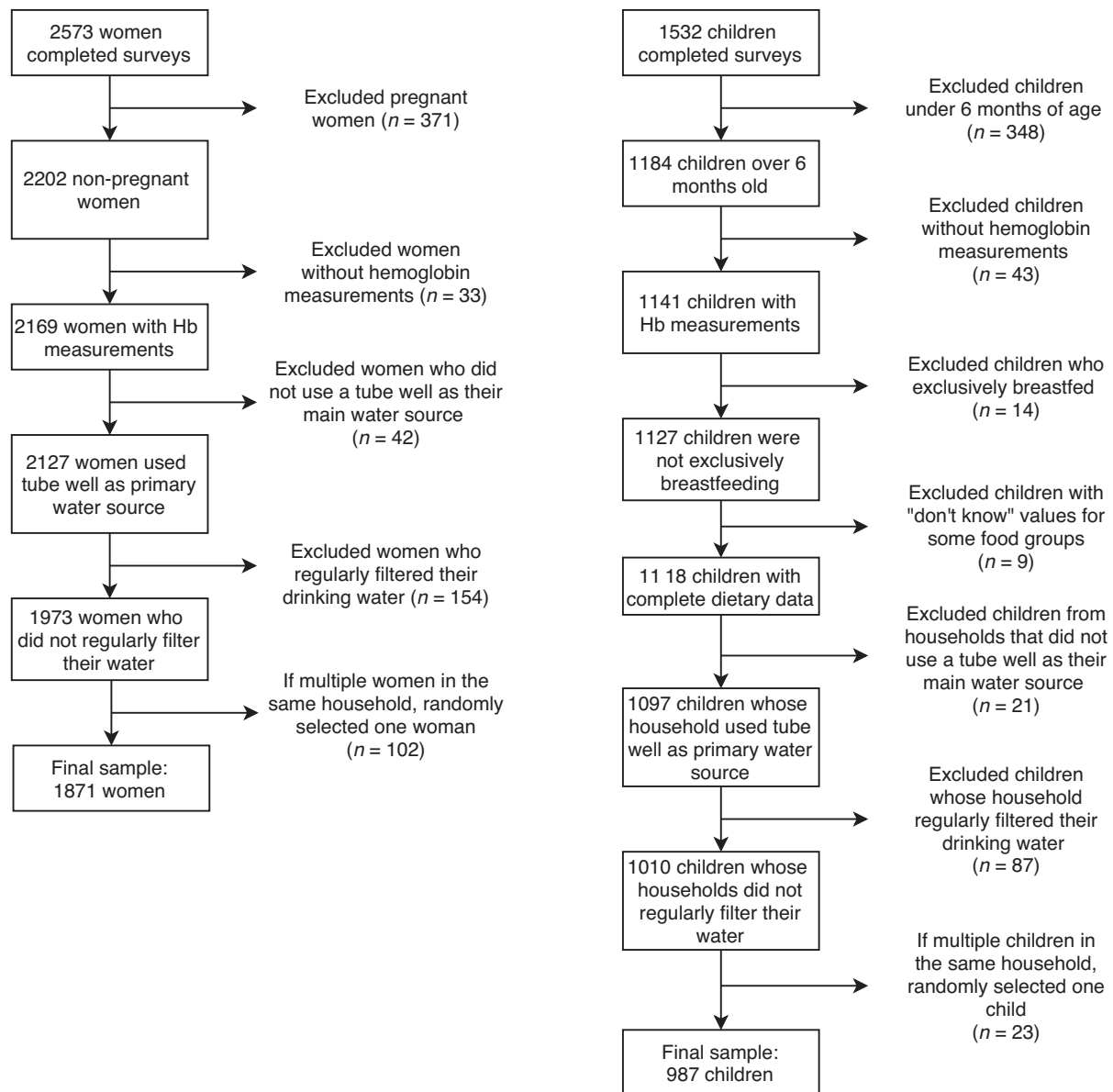
### Ethics

Study protocols were approved by the Bangladesh Medical Research Council and the James P Grant School of Public Health at BRAC University in Bangladesh and by Heidelberg University in Germany. All participants gave written informed consent before data collection.

## Results

### Sample characteristics

Overall, 34% of the women (mean Hb: 12.4 g/dL) and 51% of the children (mean Hb: 10.8 g/dL) in our analytic sample were anemic, most with mild or moderate anemia. Only about one-third of women (28%) and children (33%) in this sample ate diets that were adequately diverse. During the previous day, the majority of women consumed foods containing heme iron (80%), usually fish (78%), and one-half of the women ate vitamin C-rich fruits or vegetables (51%). Fewer children consumed iron-rich foods (44%) or vitamin C-rich foods (31%). Although exclusively breastfed children were not included in the analysis, 90% of the children (aged 6–37 mo) continued breastfeeding to some degree. Thirty-six percent of women had chronic energy deficiency (BMI  $< 18.5$ ) and 15% were of short stature ( $< 145$  cm).



**FIGURE 1** Flowchart of women and children included in the analysis in Sylhet, Bangladesh. Hb, hemoglobin.

Any iron and folic acid (IFA) supplement intake in the previous 3 mo was reported by 12% of women. Almost one-half of children were moderately or severely stunted (48%) and 11% were moderately or severely wasted ([Table 1](#)).

#### Groundwater iron

Forty-five percent of the households reported some amount of iron in their main drinking water source, with 10% reporting “a lot” of iron. In households where women reported any groundwater iron, both women and children had significantly lower odds of being anemic than in those reporting no groundwater iron ([Table 2](#)).

#### Anemia

Among women, the trend over the 4 iron perception categories (none, a little, a medium amount, a lot) to anemia was highly significant ( $P = 0.002$ ). This dose–response relation in particular appeared among

women with iron-poor or vitamin C–poor diets ([Figure 2A, B](#)). In contrast, we analyzed groundwater iron among children as a binary variable (none compared with any groundwater iron). A likelihood ratio test comparing continuous with categorical measures of groundwater iron in children showed evidence against a linear trend (better model fit with categorical variable vs. a linear effect over 4 categories:  $P = 0.03$ ) and no additional gain from using 4 categories over a binary relation ( $P = 0.56$ ). In addition, no dose–response relation was seen among children consuming vitamin C–poor diets; in contrast, they fell into 2 distinct groups ([Supplemental Figure 2](#)).

#### Dietary factors: crude associations with anemia

There was some evidence that consumption of heme-iron foods (red meat, poultry, organ meat, fish) ( $P = 0.07$ ) and of vitamin C–rich fruits or vegetables ( $P = 0.04$ ) was associated with less anemia in women ([Table 2](#)). Achieving minimum dietary diversity showed no association

**TABLE 1** Characteristics of nonpregnant women and children aged 6–37 mo in Sylhet, Bangladesh<sup>1</sup>

Characteristic	Women (n = 1871)	Children (n = 987)
Hemoglobin, g/dL	12.4 ± 1.2	10.8 ± 1.3
Anemia <sup>2</sup>		
None	66.5	48.9
Mild	23.0	28.6
Moderate	10.2	21.9
Severe	0.3	0.6
Perceived groundwater iron		
None	55.6	55.0
A little	22.9	24.5
Medium	11.9	10.6
A lot	9.6	9.8
Adequate dietary diversity <sup>3,4</sup>	27.9	32.9
Consumed vitamin C-rich foods <sup>4</sup>	50.7	31.1
Vitamin C-rich vegetables	43.8	21.7
Vitamin C-rich fruits	13.1	12.5
Consumed heme-iron foods <sup>4,5</sup>	80.3	44.2
Meat or poultry	7.6	5.5
Organ meat	1.2	2.2
Fish	78.1	38.9
Consumed nonheme-iron foods <sup>4</sup>	45.3	36.1
Dark green leafy vegetables	27.0	15.4
Legumes and nuts <sup>6</sup>	24.9	26.3
Consumed IFA supplements in the previous 3 mo <sup>7</sup>	11.5	–
Consumed iron-fortified foods	–	2.2
Consumed multiple micronutrient powder	–	0.6
BMI <sup>8</sup>	19.9 ± 3.0	–
Chronic energy deficiency (BMI <18.5) <sup>8</sup>	36.1	–
Short stature (height <145 cm)	15.0	–
Moderate/severe stunting (LAZ <–2 SD)	–	47.6
Moderate/severe wasting (WLZ <–2 SD)	–	10.9
Woman's age, y		
15–19	8.9	–
20–24	38.5	–
25–29	37.5	–
≥30	15.1	–
Child's age, mo		
6–11	–	20.5
12–23	–	42.6
23–37	–	37.0
Woman's/mother's education		
None	18.3	17.9
Any primary	46.8	45.8
Any secondary or more	34.9	36.3
Household wealth quintile		
First (poorest)	28.7	27.2
Second	23.9	24.8
Third	18.9	20.1
Fourth	16.8	16.9
Fifth (richest)	11.7	11.0
Religion		
Muslim	67.0	67.3
Hindu	33.0	32.7

<sup>1</sup>Values are means ± SDs or percentages. BMI in kg/m<sup>2</sup>. For some variables, total *n* is smaller due to missing data (IFA supplementation: *n* = 1704; BMI: *n* = 1768; stunting: *n* = 985). Final models included totals listed (women: *n* = 1870; children: *n* = 986). IFA, iron and folic acid; LAZ, length-for-age z score; WLZ, weight-for-length z score.

<sup>2</sup>Anemia cutoffs for women were mild: 11.0–11.9 g/dL, moderate: 8.0–10.9 g/dL, severe: <8.0 g/dL; and for children were mild: 10.0–10.9 g/dL, moderate: 7.0–9.9 g/dL, severe: <7.0 g/dL.

<sup>3</sup>For women, adequacy was defined as 5 or more food groups out of 10, in line with the minimum dietary diversity for women guidelines (25). For children, adequacy was defined as 4 or more food groups out of 7, in line with the WHO IYCF indicator guidelines (26).

<sup>4</sup>Consumed in the previous 24 h.

<sup>5</sup>For children, heme-iron foods include iron-fortified foods in accordance with the WHO Infant and Young Child Feeding indicator guidelines.

<sup>6</sup>The women's category included beans, peas, and lentils; the children's category included legumes and nuts.

<sup>7</sup>IFA data were collected retrospectively during surveillance (September 2015).

<sup>8</sup>BMI was only calculated for women >2 mo postpartum.

**TABLE 2** Crude associations of groundwater iron and dietary factors with anemia in women and children in Sylhet, Bangladesh

Characteristic	Women (n = 1871)			Children (n = 987) <sup>1</sup>		
	Crude OR	95% CI	P value	Crude OR	95% CI	P value
Perceived iron in water						
None	Ref			Ref		
A little	0.83	(0.66, 1.04)	0.10	0.56	(0.40, 0.77)	<0.001
Medium	0.66	(0.47, 0.93)	0.02	0.60	(0.39, 0.92)	0.02
A lot	0.63	(0.44, 0.92)	0.02	0.61	(0.38, 1.00)	0.05
Perceived iron in water (binary)						
Any vs. none	0.74	(0.60, 0.90)	0.003	0.58	(0.44, 0.76)	<0.001
Adequate dietary diversity <sup>2,3</sup>	0.92	(0.73, 1.15)	0.47	0.94	(0.73, 1.21)	0.62
Consumed vitamin C-rich foods <sup>3</sup>	0.82	(0.69, 0.99)	0.04	0.96	(0.73, 1.28)	0.80
Consumed heme-iron foods <sup>3,4</sup>	0.78	(0.59, 1.02)	0.07	0.92	(0.68, 1.24)	0.58
Consumed nonheme-iron foods <sup>3,5</sup>	0.93	(0.76, 1.14)	0.49	1.06	(0.80, 1.41)	0.68
Consumed IFA supplements in previous 3 mo <sup>6</sup>	0.89	(0.62, 1.28)	0.52	–	–	–

<sup>1</sup>All associations were adjusted for child age because this greatly influenced the associations between dietary variables and anemia. IFA, iron and folic acid.

<sup>2</sup>For women, adequacy was defined as 5 or more food groups out of 10, in line with the minimum dietary diversity for women guidelines (25). For children, adequacy was defined as 4 or more food groups out of 7, in line with the WHO IYCF indicator guidelines (26).

<sup>3</sup>Consumed within the previous 24 h.

<sup>4</sup>Heme-iron foods include fish, poultry, meat, or organ meat for both women and children. For children, heme-iron food consumption also includes any iron-fortified foods.

<sup>5</sup>Nonheme-iron foods include dark green leafy vegetables (all), legumes (women), and beans/peas (children).

<sup>6</sup>n = 1702, data were collected retrospectively during surveillance (September 2015).

with anemia in women, nor did consumption of nonheme-iron foods or consumption of any IFA supplements in the previous 3 mo (Table 2).

In children, there was strong evidence ( $P < 0.001$ ) in the crude analysis that adequate dietary diversity and consumption of iron-rich foods were associated with less anemia. Children who consumed vitamin C-rich foods were also less anemic ( $P = 0.05$ ), whereas consumption of nonheme-iron foods showed no association with anemia (data not shown). These associations disappeared when controlling for age (Table 2).

### Adjusted associations with anemia of groundwater iron, dietary factors, and their interaction

In the multivariable models, we found significant interactions between groundwater iron and dietary factors on anemia (Supplemental Table 2). Among women who did not consume vitamin C-rich foods, the odds of anemia reduced with increasing concentrations of groundwater iron ( $P$  value for trend over categories:  $<0.001$ ) (Table 3; Figure 2A). The same trend was seen for women who did not eat heme-iron foods ( $P < 0.001$ ) (Table 3; Figure 2B). Increasing groundwater iron content was less strongly associated with decreasing odds of anemia among women who consumed vitamin C-rich foods or heme-iron foods (Table 3; Figure 2A, B).

Among children, an interaction was found between groundwater iron and vitamin C-rich food consumption (Supplemental Table 3). For those not consuming vitamin C-rich foods, the presence of groundwater iron in the household was associated with reduced anemia (OR: 0.68; 95% CI: 0.50, 0.92). For those also consuming vitamin C, the odds of anemia were even lower (OR: 0.48; 95% CI: 0.32, 0.71) as compared with children with no groundwater iron nor consuming vitamin C. For those living in households without groundwater iron, consuming vitamin C was not associated with anemia (Table 4). In contrast, iron-rich food intake was not significantly associated with anemia in children, even in households with no reported groundwater

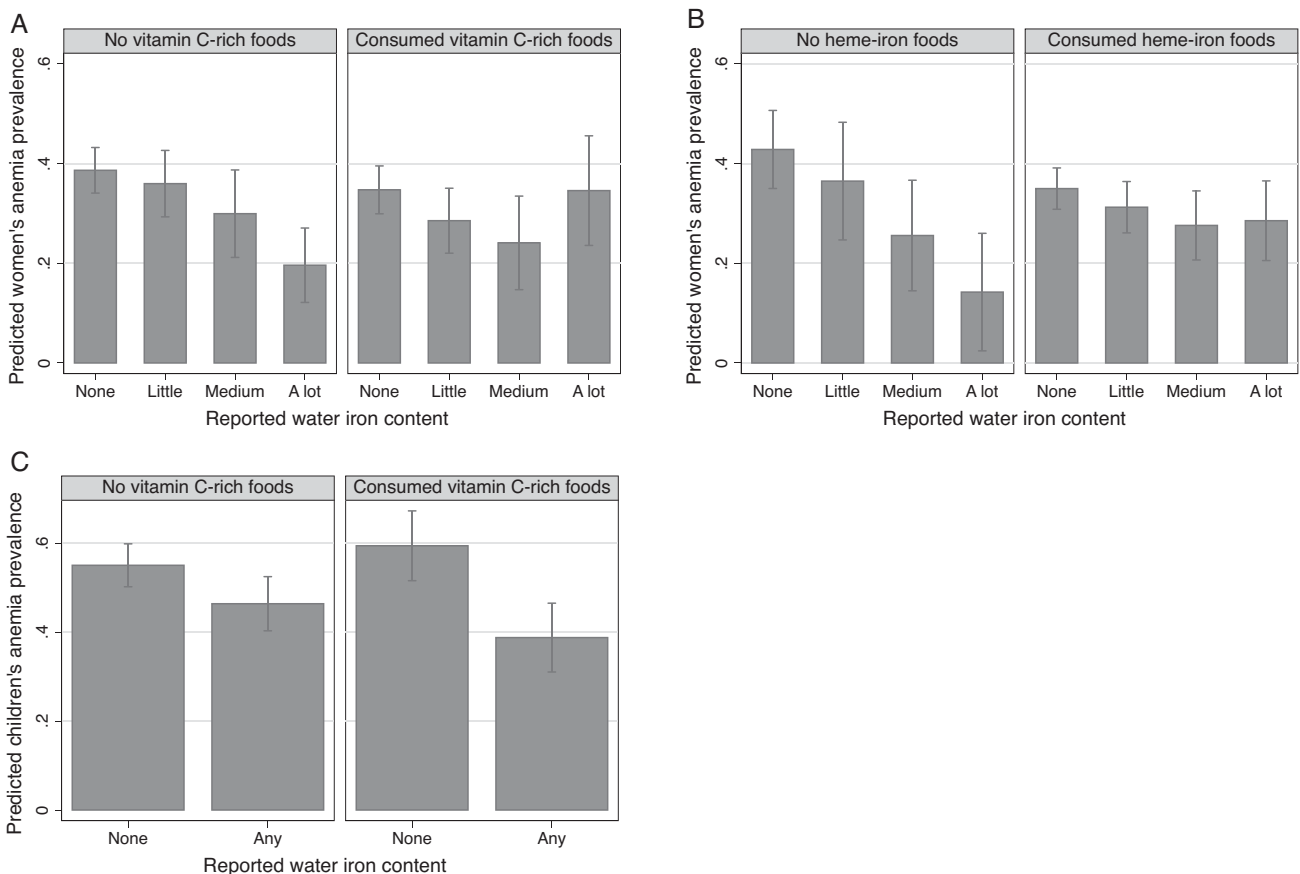
iron, and there was no evidence of an interaction (Table 4; Supplemental Table 3).

Of note, even among children who consumed groundwater iron and vitamin C-rich foods, or groundwater iron and iron-rich foods, anemia prevalence was still 39% and 46%, respectively (Figure 2C). Among women, the lowest predicted anemia prevalence was also found for those consuming groundwater iron along with vitamin C-rich foods (29%) or heme-iron foods (30%), adjusting for household wealth, pregnancy history, education, and dietary diversity. For women and children in households with groundwater iron who reported both heme-iron and vitamin C-rich food consumption, anemia prevalence continued to be elevated at 28% and 39%, respectively. Finally, if all households had reported no groundwater iron (calculated through population attributable fractions), the prevalence of anemia among women and children would be 9% higher.

### Discussion

In our study population in rural northeast Bangladesh, groundwater iron from domestic tube wells was associated with less anemia in women and children. This groundwater iron effect was modified by dietary factors. Among women, the effect was attenuated by consumption of heme-iron foods and by consumption of vitamin C-rich fruits or vegetables. In children, consuming vitamin C-rich foods strengthened the effect of groundwater iron on anemia, whereas there was no interaction of groundwater iron with consumption of iron-rich foods (heme or nonheme). Among women with iron-poor or vitamin C-poor diets, we found a dose-response effect in which anemia reduced stepwise with increasing groundwater iron concentrations.

The unexpected difference between women and children concerning the direction of the interaction may be due in part to the different prevalences of anemia found in women (34%) and children (51%),



**FIGURE 2** Predicted probabilities of anemia in women and children in Sylhet, Bangladesh. (A) Predicted probabilities of anemia in women, by reported water iron content and vitamin C-rich food consumption in Sylhet, Bangladesh ( $n = 1870$ ). (B) Predicted probabilities of anemia in women, by reported water iron content and heme-iron food consumption in Sylhet, Bangladesh ( $n = 1870$ ). (C) Predicted probabilities of anemia in children, by reported water iron content and vitamin C-rich food consumption in Sylhet, Bangladesh ( $n = 986$ ). Adjusted regression models for women included variables on household wealth, pregnancy history, education, and dietary diversity. Adjusted models for children included household wealth, maternal education, child age, and child dietary diversity.

which may signal differing levels of iron deficiency anemia (IDA). In women, dietary factors (heme iron, vitamin C) alone and groundwater iron alone were associated with reduced odds of anemia, although both together did not reduce anemia any further. This may be because there was little IDA left to address in women, although iron stores may have increased further. Children appeared to have benefitted more from a combination of factors, which is in line with them having comparatively more IDA. There being greater iron deficiency in children than in women was supported by our analysis of iron status in a subsample (results are forthcoming in another article).

Another explanation for the divergent interactions found between women and children concerning vitamin C consumption may be the differing diets of women and children. Previous evidence indicates that the typical rural Bangladeshi diet does not provide adequate iron for women or children (3). Although only one-third of both women and children reported a diverse diet, women were much more likely to consume iron-rich foods (both heme and nonheme iron) than children (Table 1). In addition, the amount of iron-rich foods consumed, which is not measured in a dietary diversity module, would likely be larger for women than for young children. Therefore, in the absence of groundwater iron consumption, women consuming vitamin C may

have been more able to access the nonheme iron in their diets. However, among children, enhancing iron absorption by vitamin C consumption alone may not have helped because they likely ate iron-rich foods in lower quantities and with lower frequencies.

For children, who may not be eating significant dietary sources of nonheme iron, groundwater may have been their main nonheme-iron source, even though their water intake is likely much lower than that of women, and vitamin C-rich food consumption may have helped make this source more bioavailable (17–19). This effect only occurs when both iron and vitamin C sources are consumed together (18). In the case of high-phytate (>250 mg) meals, common in Bangladesh (32, 33), greater amounts of vitamin C are required to compensate for the iron inhibitors present (19, 34, 35). We found that the stronger groundwater iron effect among children consuming vitamin C-rich foods was predominantly driven by vitamin C-rich fruit (compared with vegetables) (results not shown). It is possible that fruits were consumed as snacks together with water, maximizing iron absorption without the presence of iron inhibitors (e.g., phytates, tannins) often contained in full meals.

A dose-response relation was found between groundwater iron and anemia only in women who did not consume heme-iron or vitamin C-rich foods. This may be due to differing anemia etiologies between

**TABLE 3** Adjusted associations of groundwater iron and vitamin C-rich or heme-iron food consumption with anemia in women in Sylhet, Bangladesh<sup>1</sup>

	Groundwater iron	OR	95% CI	P value
Vitamin C consumption <sup>2</sup>				
None	None	Ref <sup>3</sup>	–	–
None	A little	0.89	(0.65, 1.23)	0.49
None	Medium	0.67	(0.44, 1.04)	0.07
None	A lot	0.38	(0.23, 0.63)	<0.001
Any	None	0.84	(0.66, 1.07)	0.17
Any	A little	0.63	(0.44, 0.90)	0.01
Any	Medium	0.50	(0.29, 0.84)	0.01
Any	A lot	0.84	(0.49, 1.44)	0.52
Heme iron consumption <sup>2</sup>				
None	None	Ref <sup>4</sup>	–	–
None	A little	0.76	(0.43, 1.35)	0.35
None	Medium	0.45	(0.23, 0.88)	0.02
None	A lot	0.21	(0.08, 0.60)	0.003
Any	None	0.71	(0.49, 1.03)	0.07
Any	A little	0.60	(0.42, 0.85)	0.004
Any	Medium	0.50	(0.32, 0.78)	0.002
Any	A lot	0.52	(0.31, 0.88)	0.01

<sup>1</sup>*n* = 1871. Both models were adjusted for household wealth, pregnancy history, education, and dietary diversity.

<sup>2</sup>Consumed within the previous 24 h.

<sup>3</sup>Reference category is women not consuming vitamin C-rich foods or groundwater iron. *P* values for interaction terms are the following: a little groundwater iron \* vitamin C consumption: 0.47, a medium amount of groundwater iron \* vitamin C consumption: 0.70, a lot of groundwater iron \* vitamin C consumption: 0.002.

<sup>4</sup>Reference category is women not consuming heme-iron foods or groundwater iron. *P* values for interaction terms are the following: a little groundwater iron \* heme-iron food consumption: 0.76, a medium amount of groundwater iron \* heme-iron food consumption: 0.21, a lot of groundwater iron \* heme-iron food consumption: 0.02.

women who did and women who did not consume such foods. Women who did not consume heme iron or vitamin C (which would enhance nonheme-iron absorption) may be more likely to have IDA and because they have fewer dietary iron sources, their primary source of iron would be groundwater. This would explain why the groundwater iron to anemia relation was more prominent in this subset of women. In children, a dose-response relation was not seen with increasing groundwater iron. This may be partly due to varying water consumption levels and iron needs across the child ages included in our analysis, whereas women's water consumption may be more uniform. This was supported by an analysis conducted in a subsample, which showed women's water consumption did not vary by perceived groundwater iron category (results are forthcoming in another article).

Although some women and children had dietary iron and high groundwater iron intake, anemia levels were high even in these subgroups. Among women and children who reported groundwater iron intake as well as consumption of both heme-iron and vitamin C-rich foods, anemia prevalence was still 29% and 40%, respectively. Such prevalence levels of anemia are still considered moderate and severe public health problems (1). Because iron intake (through groundwater) in these groups may already be quite high, anemia is unlikely to be addressed by iron supplementation alone. Anemia levels may also rise in the coming years if water filter use increases. This may happen due to taste preference but also to reduce arsenic content, a continuing issue in the region (36). We estimate that a reduction in groundwater iron content may lead to an ~10% increase in estimated anemia prevalence for both women and children, provided dietary patterns do not change.

Our findings support previous studies which found that elevated groundwater iron intake was linked to less anemia (10, 13, 15) and better iron status (13–15) among women in Bangladesh. Similarly, in Cambodia, elevated groundwater iron has also been reported and proposed as an explanation for the low iron deficiency prevalence in this region (37). We also found that heme-iron food consumption

**TABLE 4** Adjusted associations of groundwater iron and vitamin C-rich or heme-iron food consumption to anemia in children in Sylhet, Bangladesh<sup>1</sup>

Characteristic	OR	95% CI	P value
Groundwater iron and vitamin C-rich food consumption			
Vitamin C consumption <sup>2</sup>			
None	Ref <sup>3</sup>	–	–
None	0.68	(0.50, 0.92)	0.01
Any	1.22	(0.84, 1.78)	0.29
Any	0.48	(0.32, 0.71)	<0.001
Groundwater iron and heme-iron food consumption <sup>4</sup>			
Consumed heme-iron foods <sup>2,5</sup>	0.95	(0.68, 1.33)	0.78
Groundwater iron			
None	Ref	–	–
Any	0.57	(0.44, 0.75)	<0.001

<sup>1</sup>*n* = 987. Both models were adjusted for household wealth, maternal education, child age, and child dietary diversity.

<sup>2</sup>Consumed within the previous 24 h.

<sup>3</sup>Reference category is children not consuming vitamin C-rich foods or groundwater iron. *P* value for the interaction term is 0.03 (Supplemental Table 3).

<sup>4</sup>Margins are displayed because the groundwater iron by heme-iron food interaction was not statistically significant (Supplemental Table 3).

<sup>5</sup>Heme-iron food consumption includes consumption of iron-fortified foods or micronutrient powders.



was associated with less anemia even when adjusting for groundwater iron, an association reported as nonsignificant or borderline in 2 other Bangladeshi populations (10, 38). This may be due to the higher groundwater iron content in the study site of Merrill et al. (10) than in the FAARM trial area and to a much smaller sample size in that study ( $n = 207$ ), leading to wide CIs. Two additional studies with a larger sample size ( $n = 522$ ) in a setting with lower groundwater iron content also found no or borderline associations between red meat consumption and anemia (15, 38). However, both analyses further adjusted for iron status, which is on the causal pathway between dietary iron and anemia/Hb. This may, therefore, explain the weaker associations. No previous studies to our knowledge have examined vitamin C-rich fruit or vegetable consumption in the presence of elevated groundwater iron or studied the interaction of dietary factors with groundwater iron.

One limitation of our study is that we did not measure the iron content of tube well water at baseline or the amount of water consumed per day. We therefore used perceived iron content at that point in time. Although there is of course some misclassification in subjective reports, we showed that measured and perceived iron were highly correlated using a later measurement (Supplemental Table 1). Despite the bias to the null resulting from nondifferential misclassification, we were able to see a relation between groundwater iron and anemia. When assessing groundwater iron, Merrill et al. (14) measured iron content of water at 2 time points and averaged these to account for possible seasonal changes in iron content. Although we only asked once, it is likely that our study respondents were describing an average iron content of their main drinking water source.

Our dietary data collection methods differed from previous studies (10, 13); we used intake in the past 24 h and not 7-d food frequency, leading to more variation. We also did not estimate the exact amount of foods consumed. However, we were still able to find associations between dietary consumption, groundwater iron, and anemia status. We did not measure iron status or other biomarkers in the full baseline population, and therefore were not able to present relations of these with iron deficiency for the full sample. We did however measure iron biomarkers in a subsample and further analyses are underway.

Our study results highlight 2 important issues with relevance for policy and further research. First, vitamin C consumption appears to be a key factor which may enhance iron absorption from groundwater among children. Increasing children's consumption of vitamin C-rich fruits and vegetables may thus benefit children who consume groundwater with high iron content but are still not absorbing enough iron to improve anemia. Second, even women and children who consumed groundwater iron and diets containing heme-iron or vitamin C-rich foods still had a moderately high anemia prevalence. It is likely that this remaining anemia is not primarily due to iron deficiency but rather may be caused by nonnutritional factors such as hemoglobinopathies (10). The main drivers of anemia in this population remain to be identified.

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