Original Article

High prevalence of anemia with lack of iron deficiency among women in rural Bangladesh: a role for thalassemia and iron in groundwater

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Iron deficiency was absent in a recent population assessment of rural Bangladeshi women exhibiting anemia (57%), suggesting other causes of low hemoglobin. We assessed the relative influence on anemia of thalassemia, groundwater arsenic and iron, and diet among women of reproductive age living in rural Bangladesh. Women (n=207) sampled from a previous antenatal nutrient intervention trial in rural Bangladesh were visited during two seasons in 2008. Collected data included 7-day dietary and 24-hour drinking water intake recalls, 7-day morbidity recall, anthropometry, and drinking water arsenic and iron concentrations. Capillary blood was analyzed for iron (plasma ferritin, soluble transferrin receptor), inflammation (C-reactive protein) and thalassemia (β thalassemia and Hb E) status. In stratified, adjusted analyses, only parity was associated with anemia (odds ratio, OR (95% CI): 11.34 (1.94, 66.15)) for those with thalassemia (28% prevalent). In contrast, groundwater iron intake (>30 mg/d, 0.48 (0.24, 0.96)) and wasting (2.32 (1.17, 4.62)) were associated with anemia among those without thalassemia. Elevated groundwater arsenic (>=50 µg/L, 12% of tubewells) and a diverse diet were unrelated to anemia regardless of thalassemia diagnosis (p>0.70 and >0.47, respectively). Among women in this typical rural Bangladeshi area, the prevalence of thalassemia was high and, unlike iron deficiency which was absent most likely due to high iron intake from groundwater, contributed to the risk of anemia. In such settings, the influence of environmental sources of iron and the role of thalassemias in contributing to anemia at the population level may be underappreciated.

Key Words: Bangladesh, anemia, iron-deficiency, thalassemia, women

INTRODUCTION

Women of reproductive age experience a disproportionately higher risk for anemia with 30% of non-pregnant and 42% of pregnant women being affected.1 Iron deficiency, the most common cause of anemia, is assumed to be responsible for approximately 50% of all cases. In Bangladesh, surveys over the past 10 years have estimated the prevalence of anemia among women of reproductive age to range from 23% to 95%, depending on age, pregnancy status, and urban versus rural residency.2-11 Recent surveys have provided additional data on iron status leading to estimates that iron deficiency may be the cause of 7% to 60% of anemia in the country suggesting variability in the relative contribution of insufficient iron status to the burden of anemia.3-5 Other common causes of low hemoglobin include additional nutritional deficiencies,12 parasitic infections,13,14 chronic inflammatory conditions,15 and genetic disorders of hemoglobin synthesis and metabolism, such as thalassemia.16 Often, populations may be exposed to multiple causes, though rarely all.

Thalassemia, a group of anemias caused by genetic mutations which negatively impact erythrocyte production, and Hemoglobin E (Hb E), a hemoglobin variant, can be severe and a cause of fetal death or can be a mild, nearly symptom free condition.17 Together, Hb E and α and β thalassemias are the most prevalent forms of thalassemias and associated hemoglobinopathies; compound Hb E/β thalassemia is the most common and serious form in South Asia.18 Estimates of the prevalence of thalassemia within Bangladesh are rare.19 In general, the current evidence in South Asia, especially in Bangladesh, is in-

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Anemia influenced by thalassemia, groundwater iron

Adequate for assessing the role of thalassemia in anemia. Exposure to arsenic, known to occur across Bangladesh through intake of contaminated groundwater, has been found to increase risk of anemia by destabilizing cell membranes and decreasing erythrocyte survival. However, findings from epidemiological studies are equivocal about the strength of this association. In a study conducted in 2008 among women of reproductive age in rural northwestern Bangladesh, we observed a surprisingly high prevalence of anemia (57%) in the absence of iron deficiency (0% with plasma ferritin <12 µg/L). Understanding the epidemiology of anemia with an apparent lack of iron deficiency in this setting, typical of rural Bangladesh, is critical for the design and implementation of effective anemia prevention and treatment programs. We sought to examine the roles of several factors influencing anemia among this rural population including dietary intake patterns of bioavailable iron sources, mineral exposures from groundwater, and thalassemia.

MATERIALS AND METHODS

Data was collected in 2008 during two seasonal rounds: May to July, round 1, dry/early monsoon season, and October to November, round 2, post-monsoon season. Details of the study have been described elsewhere. In brief, eligible participants were a group of women (n=321) sampled from a biochemical sub-study (5% of the study-defined community sectors (n=32/596) nested within a larger community-based maternal vitamin A or betacarotene supplementation trial. Participants were eligible if during the original trial, called “JiVitA-1”, 1) their enrolled pregnancy ended in a live birth; 2) they maintained the same residence; and 3) their trial database included complete iron and infection status information. Two additional criteria were imposed in 2008 prior to the start of data collection: current residence in the study area and not being pregnant. Pregnancy at enrollment was an exclusion criterion because of the planned blood sample collection for biochemical status assessment 4 to 6 months later in round 2, and the known influence of pregnancy on iron status. However, becoming pregnant between rounds 1 and 2 was recorded but not an exclusion criterion. All interviews and assessments were conducted at the participant’s home by locally-hired, JiVitA Project-trained female staff.

Interviews

In both rounds, participants were asked about their dietary intake using a 7-day, 42-item food frequency questionnaire (FFQ). Twenty-four hour drinking water and rice intake data was gathered using semi-quantitative recalls with six meal and between-meal time prompts. The unit of measurement for the drinking water recall was a participant-identified usual drinking container, the volume (±10 mL) of which was measured during the interview using a calibrated 500 mL measuring cup. Recent morbidity was assessed with a 7-day morbidity recall. Information on pregnancy history since participation in the original trial and current socioeconomic status (SES) was collected in round 1 using interview modules abbreviated from those employed in JiVitA-1 for consistency.

Anthropometric status was recorded in round 1 by measuring weight (±0.1 kg) with a digital UNICEF Uniscal (SECA, Gmb & Co, Hamburg, Germany), height (±0.1 cm) using a JiVitA Project-constructed, portable stadiometer, and mid-upper arm circumference (MUAC, ±0.1 cm) using a non-stretch, locally manufactured insertion tape. All interviewers were trained and standardized in standard anthropometric methods before data collection.

In brief, tubewells were purged of any residual minerals on the inside of the pipe and the aquifer source was reached by pumping a steady stream of water for 5 minutes. Subsequently, a water sample collected directly from the tubewell water flow was analyzed for total iron concentration using a previously validated, field-based, colorimetric iron test kit (±0.1 mg/L, HACH Iron Test Kit, Model IR-18B). Simultaneously, a water sample was analyzed for arsenic concentration (category of µg/L, Visual Arsenic Detection Kit, Wagtech International Ltd, Berkshire, UK).

Iron status

In round 2, a capillary blood sample (300 µL, EDTA coated, Safe-T-Fill, RAM Scientific, Inc, Yonkers, NY, USA) was collected and immediately stored in an insulated cool bag until same-day processing at the Project laboratory in Gabtandha. Plasma aliquots were immediately stored in liquid nitrogen until ferritin (µg/L), soluble transferrin receptor (TfR, mg/L), and C-reactive protein (CRP, mg/L) analysis at the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR, B) in Dhaka by a sandwich ELISA method described elsewhere by Erhardt et al. ICDDR, B used Roche standards (Roche Diagnostics, Roche, Switzerland) to obtain the calibration curves. Red blood cells, washed 3 times with saline, were stored in liquid nitrogen until analysis for β thalassemia and Hb E status at the Dhaka Shishu Hospital Thalassemia Center using acateate gel electrophoresis with A2 hemoglobin fraction quantification performed by densitometry (Gel alkaline Hb SAS, MX manual electrophoresis unit, Helena BioSciences, UK). Hemoglobin concentration (Hb, g/L, B-Hemoglobin HemoCue photometer, HemoCue Inc, Mission Viejo, CA, USA, checked daily for accuracy) was assessed on the spot at the time of blood sample collection. HemoCue microcuvettes were used within 10 days of opening the bottle which was stored at 4°C overnight.

Statistical analysis

Anthropometric variables were dichotomized to define general wasting: BMI <18.5 kg/m² or mid-upper arm circumference (MUAC) <21.5 cm. Recent morbidity in round 2 at the time of blood sample collection was classified as a binary variable representing any report in the previous 7 days of high fever, vomiting, painful urination, dysentery, or diarrhea. Five food groups were defined as follows: red meat (meat and liver), chicken and fish, dark green leafy vegetables, fruits, and dairy and eggs. Food group intake frequency in each round and as a mean of
both rounds was categorized as 0 to 2 or ≥3 times per week. Additionally, a diverse diet was defined by consuming ≥3 food groups regularly (≥3 times per week).

To account for seasonal fluctuation in groundwater iron concentration, mean round 1 and 2 values, combined with mean daily drinking water consumption, was used to define groundwater iron intake (mg/day). Mean daily groundwater iron intake from drinking was dichotomized at >30 mg, a common iron supplement dose. Mean category of arsenic concentration was dichotomized at the Bangladesh government defined limit of 50 µg/L.32

The following definitions were applied to biochemical indicators to define abnormality: anemia, Hb ≤120 g/L and 110 g/L for non-pregnant and pregnant women (n=8 were in their 1st trimester of pregnancy at the time of assessment), respectively,33 moderate anemia, ≤90 g/L; severe anemia, ≤70 g/L; iron deficiency, plasma ferritin <12 µg/L or TIR >8.5 mg/L; iron deficiency anemia, the presence of anemia and iron deficiency; and, subclinical infection, CRP >5.0 mg/L.34

Differences in baseline demographic characteristics, socioeconomic status (SES) and anthropometric measures were assessed by study participation. Hemoglobin concentration and prevalence of anemia were compared by iron, subclinical infection and thalassemia status, recent morbidity, intake of various food groups, daily iron intake through drinking water, and drinking water arsenic concentration using z-test for proportions, Fisher’s exact test for multiple category variables, and Student’s t-test or one way analysis of variance (ANOVA) for continuous distributions.

Logistic regression was used to assess the crude association between the risk of anemia and demographic and biochemical characteristics, as well as mean dietary and groundwater mineral intake patterns. Covariates exhibitng an association with anemia (p<0.10) were included when developing multivariable logistic regression models. Model fit was assessed using Akaike’s information criterion (AIC) and log likelihood ratio tests to ensure a parsimonious model. Results did not differ between those who were and were not pregnant and, therefore, all participants were included in the analyses regardless of pregnancy status.

All analyses were performed using STATA statistical software package version 11.0.35

The study was approved by the Bangladesh Medical Research Council, Dhaka, Bangladesh and the Committee on Human Research at the Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD.

RESULTS

Of the 307 (96% of 321 eligible) consented participants, 20 (7%) did not participate in round 2, 64 (23%) were missing a sufficient blood sample, and 16 (5%) were missing other data. Therefore, complete data was available for 207 participants (64% of those enrolled). Baseline characteristics did not differ by inclusion status. For those with complete data, median (25th, 75th percentiles; Q1, Q3) age (yr) and parity were 24 (21, 28) and 2 (2, 3), respectively (Table 1). Mean (SD) BMI (kg/m²) and MUAC (cm) were 19.4 (2.8) and 23.8 (2.4), respectively. Forty percent (n=80) were wasted based on a low BMI. Twelve percent (n=25) had a low MUAC, all of whom also were defined as wasted based on BMI.

Mean (SD) hemoglobin (Hb, g/L) was 117 (16) (Table 1). More than half of the population (57%, n=118) was anemic, 6% (n=12) were moderately anemic, and none had severe anemia. Median (Q1, Q3) plasma ferritin (µg/L), TIR (mg/L), and CRP (mg/L) were 68 (48, 100), 2.3 (2.0, 2.9), and 0.3 (0.1, 1.2), respectively. No participants (n=0, 0%) were iron deficient, and, therefore, no participant (n=0) was classified as having iron deficiency anemia.

Subclinical infection was uncommon (7%, n=14) and was not associated with report of recent morbidity (n=38) at the time of assessment (p=0.49). Hemoglobin concentration did not differ by presence of subclinical infection or morbidity (p=0.23 and 0.37, respectively). However, the prevalence of anemia was significantly lower in those with subclinical infection (29%) in comparison to those without (59%) (p=0.03).

Seven-day intake frequency of five food groups was inconsistent across rounds. Women consumed milk and eggs more frequently in round 1 (% consuming food group ≥3 times/wk, round 1 vs round 2: 44% vs 31%, p<0.01). Red meat and chicken and fish were consumed regularly by a larger proportion of women in round 2 (6% vs 9% and 60% vs 82%, respectively, p ≤0.01). A diverse diet was more common in round 1 (30%) than round 2 (16%) (p<0.01). Hemoglobin concentration and prevalence of anemia were not associated with intake frequency of any food group or consumption of a diverse diet in either round (p=0.11). Individual mean round 1 and 2 intake patterns were also not associated with hemoglobin and anemia.

Thalassemia (β thalassemia or Hb E status) was 28% prevalent (n=57). A majority were Hb E carriers (n=48) while 6 had Hb E disease and 3 were β thalassemia carriers (Table 2). Plasma ferritin and subclinical infection did not differ by any thalassemia diagnosis (p=0.23 and 0.93, respectively). However, mean (SD) Hb concentration (g/L) was lower among those with any thalassemia (112 (16)) compared to those without (119 (16)) (p <0.01). Additionally, a diagnosis of any thalassemia or, specifically, Hb E carrier status, was associated with an increased odds of anemia (odds ratio (OR) (95% CI): 2.42 (1.25, 4.70) and 2.30 (1.14, 4.64), respectively).

Nearly two thirds of participants (63%, n=131) consumed ≥30 mg of iron/day from drinking naturally iron rich groundwater. Elevated groundwater iron intake was significantly associated with increased iron status (% (95% CI) increase in plasma ferritin: 37.4 (16.8, 61.8), p<0.001 using simple linear regression). Along this line, elevated daily groundwater iron intake was associated with 44% reduction (95% CI: 0%, 69%, p=0.05) in the odds of anemia (Table 2). After stratifying by any thalassemia diagnosis, groundwater iron intake remained significantly associated with iron status only among those with no thalassemia (% change in plasma ferritin (95% CI): 48.6 (22.8, 79.8) vs 12.2 (-18.3, 54.1) for those without and with thalassemia, respectively).

Overall, any thalassemia, parity (≥2 vs 1), and wasting undernutrition (BMI <18.5 kg/m²) were consistently associated with an increased odds and elevated daily iron
intake from groundwater a decreased odds of anemia in crude and adjusted analysis (Table 2). Among those with no thalassemia, elevated groundwater iron intake significantly reduced the odds and wasting undernutrition increased the odds of anemia. However, for those with thalassemia, there was no association between groundwater iron intake, and, parity, not wasting, was a risk factor for low hemoglobin.

DISCUSSION

Among a population of women living in rural Bangladesh with a high rate of anemia despite apparent sufficient iron status, we investigated the epidemiology of decreased hemoglobin concentration. A major finding was that 28% of assessed women had β-thalassemia or Hb E. We found a significant and consistent protective effect on anemia of an estimated consumption of more than 30 mg of iron per day from drinking iron rich groundwater, recently described by us to be a dietary source of iron that is positively associated with iron status. However, after stratifying by thalassemia status, this relationship held only among those with no diagnosis. Intake frequency of meat products, dark green leafy vegetables, and other food groups, using a 7-day food frequency recall, was not associated with the risk of anemia as was groundwater arsenic, which on average was low in this population.

It is well known that ineffective erythropoiesis due to thalassemia increases the risk of microcytic anemia, an effect that is consistent with the results of this study. Interestingly, among those with thalassemia a parity of 2 or more increased the odds of anemia by 11-fold over those with only 1 previous birth; a relationship absent among those with no thalassemia. It seems that for those with thalassemia who, consequently, have to some degree abnormal hemoglobin synthesis, the physiological demands of pregnancy are much more pronounced and reduce the ability of the body to recover in terms of hemoglobin concentration.

Paradoxically, thalassemia associated anemia can be found in the presence of iron overload as a result of iron absorption dysregulation. Along these lines, a recent study among Thai women with β-thalassemia, α-thalassemia 1, Hb E, or Hb E/β-thalassemia found that iron absorption regulation resembled rates in iron deficient anemic patients and did not properly respond to increased iron stores, and that erythrocyte incorporation of absorbed iron was lower among those with thalassemia. Although we do not have information on iron absorption rates among the current population with sufficient but not necessarily overloaded iron status, we found a definitive reduced risk of anemia associated with a daily intake of more than 30 mg of groundwater iron among those without thalassemia, however, those with thalassemia showed no significant response to this exposure. This finding

Table 1. Participant characteristics at enrollment in 2008 for those with complete data (n=207)

| Characteristic                      | Value                           | n (%) beyond cutoff
|------------------------------------|---------------------------------|-------------------
| Age (yrs)                          | n (%)                           |                   |
| <20                                | 43 (21)                         |                   |
| 20-25                              | 83 (40)                         |                   |
| 26-30                              | 55 (27)                         |                   |
| >30                                | 26 (13)                         |                   |
| Parity                             | 37 (18)                         |                   |
| 2-3                                | 130 (63)                        |                   |
| >3                                 | 40 (19)                         |                   |
| Education (yrs)                    | 77 (37)                         |                   |
| 1-9                                | 110 (53)                        |                   |
| >9                                 | 20 (10)                         |                   |
| Wealth Index                       | 51 (25)                         |                   |
| Lowest quartile                    | 48 (23)                         |                   |
| Highest quartile                   | 185 (89)                        |                   |
| Muslim                             | mean (SD)                       | n (%) beyond cutoff |
| Weight (kg)                        | 43.7 (6.8)                      |                   |
| Height (cm)                        | 150 (5.5)                       |                   |
| BMI (kg/m²)                        | 19.4 (2.8)                      | 83 (40)           |
| Mid upper arm circumference (MUAC, cm) | 23.8 (2.4)                  | 12 (25)           |
| Biochemical status                 | 117 (16)                        | 118 (57)          |
| Hemoglobin (Hb, g/L)               | 78 (47)                         | 0 (0)             |
| Plasma ferritin (µg/L)             | 2.5 (0.9)                       | 0 (0)             |
| Transferrin receptor (TfR, mg/L)   | 1.6 (4.3)                       | 14 (7)            |

1 Reasons for incomplete data: did not participate in round 2, 20 (7%); missing data, 16 (5%); insufficient or missing blood sample, 64 (23%). No difference in characteristic distribution from those with incomplete data (p>0.05).
2 Wealth index quartiles defined for entire JiVitA-1 population based on enrollment data.
3 Cut-offs defined by: wasted undernutrition, BMI <18.5 kg/m² or MUAC <21.5 cm; anemia, Hb <120 g/L and 110 for non-pregnant and pregnant women, respectively; iron deficiency, plasma ferritin <12 µg/L or TfR >8.5 mg/L; and subclinical infection, CRP >5.0 mg/L. At the time of blood sample collection, 8 (4%) participants were in the 1st trimester of pregnancy.
Table 2. Odds ratios (95% CI) of risk factors for anemia (Hb <120 g/L and 110 for non-pregnant and pregnant women, respectively) among women of reproductive age in rural Bangladesh overall, and stratified by thalassemia status

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Overall</th>
<th>Bivariate</th>
<th>Adjusted</th>
<th>β-thalassemia or Hb E diagnosis</th>
<th>None</th>
<th>Adjusted</th>
<th>Bivariate</th>
<th>Adjusted</th>
<th>Any</th>
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<tr>
<td></td>
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<td>Bivariate</td>
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<td>Bivariate</td>
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<tr>
<td>n (%)</td>
<td>207 (100)</td>
<td>150 (72)</td>
<td>57 (28)</td>
<td></td>
<td>NA</td>
<td>NA</td>
<td>0.71 (0.21, 2.43)</td>
<td>0.61 (0.15, 2.47)</td>
<td>1.72 (0.51, 5.86)</td>
<td>1.52 (0.39, 5.91)</td>
</tr>
<tr>
<td>Any thalassemia</td>
<td>2.42 (1.25, 4.70)*</td>
<td>2.48 (1.24, 4.94)*</td>
<td>NA</td>
<td></td>
<td>0.51 (0.26, 1.01)**</td>
<td>0.48 (0.24, 0.96)**</td>
<td>0.71 (0.21, 2.43)</td>
<td>0.61 (0.15, 2.47)</td>
<td>1.72 (0.51, 5.86)</td>
<td>1.52 (0.39, 5.91)</td>
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<tr>
<td>Groundwater iron intake (&gt;30 mg/d)</td>
<td>0.56 (0.31, 1.01)**</td>
<td>0.50 (0.27, 0.93)**</td>
<td>0.51 (0.26, 1.01)**</td>
<td>0.48 (0.24, 0.96)**</td>
<td>0.71 (0.21, 2.43)</td>
<td>0.61 (0.15, 2.47)</td>
<td>1.72 (0.51, 5.86)</td>
<td>1.52 (0.39, 5.91)</td>
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<tr>
<td>Undernourished (BMI &lt;18.5 kg/m²)</td>
<td>2.07 (1.16, 3.70)**</td>
<td>2.13 (1.17, 3.88)**</td>
<td>2.26 (1.16, 4.12)**</td>
<td>2.32 (1.17, 4.62)**</td>
<td>1.72 (0.51, 5.86)</td>
<td>1.52 (0.39, 5.91)</td>
<td>1.72 (0.51, 5.86)</td>
<td>1.52 (0.39, 5.91)</td>
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<tr>
<td>Parity (2 or more)</td>
<td>2.98 (1.42, 6.27)*</td>
<td>3.12 (1.45, 6.71)*</td>
<td>1.96 (0.86, 4.51)</td>
<td>2.11 (0.89, 4.99)</td>
<td>11.7 (2.04, 67.0)*</td>
<td>11.3 (1.94, 66.2)*</td>
<td>11.7 (2.04, 67.0)*</td>
<td>11.3 (1.94, 66.2)*</td>
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<tr>
<td>Groundwater arsenic (&gt;50 µg/L)†</td>
<td>0.75 (0.32, 1.76)</td>
<td>0.75 (0.26, 2.15)</td>
<td>0.61 (0.13, 2.88)</td>
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<td>Dietary factors (≥3 times/wk)</td>
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<tr>
<td>Red meat and liver</td>
<td>0.74 (0.23, 2.38)</td>
<td>0.70 (0.15, 3.24)</td>
<td>0.55 (0.08, 3.66)</td>
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<tr>
<td>Fish</td>
<td>0.55 (0.24, 1.28)</td>
<td>1.07 (0.45, 2.55)</td>
<td>NA‡</td>
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<tr>
<td>Dairy and egg</td>
<td>1.45 (0.84, 2.53)</td>
<td>1.48 (0.77, 2.82)</td>
<td>1.16 (0.36, 3.68)</td>
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<tr>
<td>Dark green leafy vegetables</td>
<td>0.77 (0.40, 1.45)</td>
<td>0.71 (0.34, 1.46)</td>
<td>1.70 (0.32, 9.02)</td>
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<tr>
<td>Fruit</td>
<td>1.07 (0.62, 1.86)</td>
<td>1.17 (0.62, 2.22)</td>
<td>1.01 (0.31, 3.22)</td>
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<tr>
<td>Diverse diet§</td>
<td>1.23 (0.70, 2.24)</td>
<td>1.30 (0.67, 2.55)</td>
<td>1.39 (0.38, 5.16)</td>
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* p ≤ 0.01  
** p ≤ 0.05  
† Missing values for 10 participants' tube wells.  
‡ Consumption of fish did not differ by thalassemia diagnosis; however, of those with thalassemia there were no participants with anemia who rarely ate fish thus preventing the ability to calculate an odds ratio.  
§ A diverse diet is defined by consuming ≥3 food groups regularly (≥3 times/week)
suggestions that those with thalassemia may have already reached a limit in iron absorption or iron incorporation in erythropoiesis from this exposure. However, it should be noted that all women included in this study were of reproductive age with at least one full term, live birth pregnancy who were up until now undiagnosed with thalassemia suggesting that they have mild forms of the disease and, consequently, experience iron absorption that may be only minimally affected if at all. Additionally, while the prevalence of the variants of thalassemia detected in this study were surprisingly high, describing associations between an exposure, ie, elevated groundwater iron intake, and an outcome, ie, anemia, among a small sample of women (n=67 with thalassemia) should be made with caution.

Intake frequency of five food groups was assessed in each data collection round using a conventional 7-day food frequency questionnaire which included known major food sources of heme and non-heme iron. To account for variability across seasons, dietary intake in each round as well as a mean of both rounds was used to describe individual patterns. The reported dietary patterns were consistent with one of modest vitamin and mineral intakes, as reported in many resource poor settings, however, were not associated with risk of anemia. The lack of association may have resulted from the adequate iron status among this population. We explored the role of wasting (BMI <18.5 kg/m²) as a proxy for possible micronutrient deficiencies in addition to inadequate protein and energy intake, and, similar to studies in India and in Bangladesh, found that this index was associated with an increased risk for anemia. However, this relationship was maintained only among those with no thalassemia. It should be noted that the limited number of participants with thalassemia may have impacted the ability to detect a significant association within that group.

The negative influence of a chronic exposure to arsenic and anemia on a population level, hypothesized to work through hemolysis and oxidative stress, is still unresolved. One study among pregnant women (n=810) in Chile found those living in a city with elevated arsenic levels in drinking water (40 µg/L) were more likely to develop anemia by 3rd trimester than those living in an area with minimal to no arsenic. A recent survey in Bangladesh (n=1954) showed that high arsenic exposure was negatively associated with Hb concentration in men and among a sub-population of women with a Hb concentration <100 g/L; however, the impact on risk of anemia was not discussed. In our study we found no association between arsenic levels in drinking water and prevalence of anemia. One limitation is that we measured this exposure indirectly rather than through more rigorous methods including arsenic metabolite concentration in urine or blood. The lack of a significant finding in the present study may be due to a) relatively low arsenic concentrations in the area’s groundwater, as shown by only 7% of tube well having an arsenic concentration above 50 µg/L, and b) the limited ability for the field kit used in this study, with a categorical, colorimetric design, to precisely quantify concentrations below 50 µg/L.

It is well known that chronic infection increases the risk of anemia; now understood to be due, in part, to increased hepcidin production associated with increased interleukin 6 (IL-6) and other infection response mechanisms leading to consequent sequester iron sequestration and decreased erythropoiesis. We found that subclinical infection, defined by elevated CRP, was uncommon and associated with a reduced risk of anemia which was attenuated after adjusting for other significant covariates. However, because of the low number of participants with elevated CRP and the incongruous association between infection and anemia that was attenuated with adjustment, these findings need to be interpreted with caution. One explanation for an inverse relationship could be that the subclinical infection captured by CRP at one time point may not reflect inflammation that has persisted long enough to impact erythropoiesis. Further, that iron sufficiency was common may have meant that a longer duration of infection would have been required to cause a decline in hemoglobin concentration to below the cut-off that defines anemia.

Along these lines and given the higher than expected iron status distribution, helminths, such as hookworm which may be common in the study area were not considered to be a substantial cause of low hemoglobin. Ma laria, another common cause of anemia, is endemic in parts of the country; however, the District of Gaibandha, where this study was conducted, is an area with minimal rates of this disease.

In conclusion, anemia prevalence was high among this population; however, in contrast to widely held assumptions that half of anemia cases are caused by inadequate iron status, this population exhibited surprising iron sufficiency in an environment where the diet is chronically low in bioavailable iron, as conventionally assessed without reference to water intake. This and previous studies in the area suggest that the iron sufficiency is most likely due to the chronic consumption of iron-rich groundwater and that a proportion of anemia may be due to an unexpectedly elevated prevalence of thalassemia and Hb E. The influence of these exposures on the prevalence of anemia at the population level may be underappreciated and should be considered when designing anemia treatment and prevention programs in similar settings typical of rural Bangladesh as they may limit the ability of iron supplementation to reduce risk. To assess the presence of these factors, programs could incorporate the use of field based groundwater iron testing kits and survey information, where available, describing expected rates of thalassemias. These findings may be generalizable to a wider region of South Asia given the ubiquitous use of groundwater sources often rich in minerals and a known high prevalence of thalassemia in populations across the greater Gangetic flood plain.

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The authors declare no conflict of interest.

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Original Article

High prevalence of anemia with lack of iron deficiency among women in rural Bangladesh: a role for thalassemia and iron in groundwater

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孟加拉鄉村地區非鐵缺乏貧血的高盛行率：地中海貧血症及地下水中鐵之角色

近期調查顯示孟加拉部分鄉村地區的婦女中非鐵缺乏的貧血盛行率達 57%，推測有其他因素造成低濃度的血色素值。本研究評估地中海貧血症、地下水中的砷及鐵、以及飲食對於孟加拉鄉村地區的育齡婦女貧血的相關影響。個案來自於先前的產前營養介入試驗的孟加拉鄉村婦女，計 207 位的參與者於 2008 年接受 2 次面訪。資料收集包括 7 天的飲食頻率問卷、24 小時飲用水攝取回憶記錄、7 天的疾病史、體位測量以及飲用水中的砷及鐵濃度。血液分析項目包括鉻(血漿儲鐵蛋白、水溶性運鐵蛋白受體)、發炎反應(C-反應蛋白)及地中海貧血症(β 地中海型貧血及血色素 E)的狀態。在分層、校正分析結果顯示只有生產次數與地中海貧血患者(盛行率 28%)的貧血有顯著相關(OR: 11.34，95% CI: 1.94, 66.15)。相反地，地下水的鐵攝取量每天高於 30 毫克(OR: 0.48，95% CI: 0.24, 0.96)及消瘦(OR: 2.32，95% CI: 1.17, 4.62)與無地中海貧血症者的貧血具有顯著相關。高的地下水砷濃度(12%的管井含量高於 50 µg/L)或多樣化的飲食與無論是否有地中海貧血診斷的貧血都不具相關。在孟加拉典型鄉村地區的婦女，由於地下水中含有高量的鐵，故缺鐵性貧血較少見；然而偏高的地中海貧血症盛行率，卻是貧血的高風險因子。在這樣的情境下，環境來源鐵的影響及地中海貧血症導致貧血的重要角色，在族群的層次上有可能是被忽視的。

關鍵字：孟加拉、貧血、鐵缺乏、地中海貧血症、婦女