Anemia and iron deficiency during pregnancy in rural Bangladesh

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Abstract

Objective: To assess the prevalence of anemia, iron deficiency and iron deficiency anemia (IDA) among pregnant women in rural Bangladesh.

Design: Baseline data on 215 pregnant women who were invited to participate in an iron supplementation trial were used. The women were in their second trimester and selected at registration from 50 antenatal care centers. Hemoglobin (Hb) concentration of venous blood samples was measured by HemoCue® system. Serum was collected for assessment of ferritin by immuno-radiometric assay and transferrin receptors (sTfR) by immunoassay double sandwich method. , Anemia was defined as having Hb concentration <110 g/L, iron deficiency as serum ferritin <12 μg/L and/or sTfR >8.5 mg/L and IDA as the combination of anemia and iron deficiency. High sTfR/serum ferritin ration was >500.

Setting: The central part of Bangladesh, in a rural area of Mymensingh district between May-November, 1997.

Results: Mean (SD) of Hb was 110 g/L (14 g/L), while median serum ferritin, sTfR and sTfR/serum ferritin was 13.7 μg/L, 6.2 mg/L and 458, respectively. The prevalence of anemia was 50%, iron deficiency 54% and high sTfR/serum ferritin 48%. None of the study women had severe anemia. The prevalence of IDA was 33%. Of the anemic women 66% had iron deficiency and 64% high sTfR/serum ferritin.

Conclusion: Both anemia and iron deficiency were highly prevalent. About two-thirds of the anemia cases were associated with iron deficiency.

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Descriptors: Anemia, iron deficiency, iron deficiency anemia, serum transferrin receptor, serum ferritin, pregnant women, Bangladesh

Introduction

Anemia during pregnancy is a significant public health problem in many parts of the world. There are large geographical variations in prevalence, but 56% of the pregnant women in developing countries are reportedly affected by anemia, in contrast to the estimated prevalence of 18% in developed countries (ACC/SCN 2000). Anemia during pregnancy is associated with a number of negative health outcomes such as preterm delivery, increased risk of low birth weight, and perinatal mortality (Scholl 1992, Godfrey 1991, Liberman 1987). Severe anemia is believed to be associated with a large proportion of maternal deaths in developing countries (Bothwell 1979).

A number of factors, such as presence of acute and chronic infections, parasite infestations, iron deficiency as well as other nutrient deficiencies may aggravate anemia among pregnant women. Of these, iron deficiency has often been identified as the predominant cause (ACC/SCN, 1991; WHO 1998). Consequently, anemia prevention and treatment strategies have mainly been based on efforts to correct iron deficiency by routine iron supplementation. Pregnant women have been recommended to start the supplementation as early as possible continuing till 6 weeks post-partum (De Maeyer 1989). However, anemia prevention and control programs have not been as effective as expected (WHO 1998). A major reason for this is deemed to be the failure in reaching all pregnant women and motivating them to take the supplements. Recently, however, it has been questioned whether iron deficiency is contributing to prevalence and severity of anemia as much as it was originally thought. Until now, few data are available on the proportion of anemia during pregnancy that can be prevented and treated by provision of iron supplements.

In different surveys in Bangladesh, the anemia prevalence among pregnant women has been estimated to be between 45% and 59% (INFS 1966, 1976, 1983, Jahan 1998, Hussain 1976, HKI 1999). However, these surveys were not primarily designed to estimate anemia prevalence in pregnant women and sample sizes were low.

Furthermore, in most of the surveys sampling procedure for pregnant women as well as the laboratory procedures to measure hemoglobin concentration were not clearly reported.

Information on etiology of anemia and severity of iron deficiency among pregnant women is much limited in Bangladesh. One study in an urban maternity clinic reported that about 86% of the anemic pregnant women had transferrin saturation <16%, indicating that iron deficiency was common (Islam 1977). Baseline information of another study conducted in urban slums reported that 23% of the non-pregnant women had signs of depleted iron stores, i.e., serum ferritin <12 μg/L (Kolsteren 1999). However, there is no community-based information available on iron deficiency and iron deficiency anemia among pregnant women in rural areas of the country.

The aim of the present study was to assess the prevalence of anemia, iron deficiency and iron deficiency anemia (IDA) among pregnant women in a rural area of Bangladesh.

Subjects and Methods

Study area

The study was conducted from May-November 1997 in a rural area of Mymensingh district, located about 110 km North West of Dhaka. The study area has high population density, plain agricultural land, low literacy rate, high prevalence of malnutriton and limited access to health services, comparable to most parts of the country. Major food crops grown in the study area include rice, wheat, beans and a variety of seasonal fruits and vegetables. The diet is dominated by rice and other foods of plant origin and is occasionally mixed with pieces of meat and fish. According to the district health office, the study area is not a malaria endemic area and there has not been any reported case of HIV.

Subjects

As part of the government policy, all pregnant women in Bangladesh are expected to receive iron tablets starting as early as possible in pregnancy and continuing until six weeks post-partum. To supplement on-going government activities, BRAC, a large national private development organization in Bangladesh, provides iron tablets to pregnant women through its community-based antenatal care centers (ANCCs). Each ANCC covers around 1000 population and is managed by a female Community Health Worker (CHW).

The data for this paper was drawn from baseline information in an iron/folate supplementation trial. For the trial, 50 of 96 ANCCs in the area had been selected based on their accessibility throughout the year. All pregnant women in the area served by the study ANCCs were identified through house-to-house visits. A total of 611 pregnant women were found. Information was collected on their socio-economic situation and reproductive history and their registration at the monthly antenatal care activities was encouraged.

The sample for the this paper consists of 215 pregnant women registering for services and having complete data on hemoglobin concentration (Hb), serum ferritin (SF) and serum transferrin receptor (sTfR). The first women fulfilling the inclusion criteria for the supplementation trial such as age of gestation less than 24 weeks and no previous iron supplementation during the current pregnancy were invited to participate. In most cases 4 women were included from each center but few centers included 5 or 6 women.

The women fulfilling the inclusion criterion were informed about the supplementation trial, what participation would involve and that they could withdraw from the trial at any time. Their consent to participate was sought. The study protocol was approved by the ethical committee of the Bangladesh Medical Research Council, Government of Bangladesh as well as by the Research Ethics Committee of the Medical Faculty, Umeå University, Sweden.

Data collection

Characteristics such as age, gestational age, parity, family size, schooling, household land ownership, perceived household economic status, and membership in BRAC rural development program were collected on all identified women through house-to-house visits. Gestational age in weeks was determined based on recall of last menstrual period. The questionnaire included three indicators of socio-economic status (SES): formal schooling of the woman, household landholding and perceived household economic status. These three indicators have been used and tested in other studies and found to be valid measures of SES in rural areas of Bangladesh (BRAC 1994). For school attendance, a woman who did not complete at least one year in a formal school was categorized as having no schooling. Households with less than 0.5 acre of land were categorized as functionally landless. This definition of landlessness has been used to target poor households for poverty alleviation programs in Bangladesh (BBS 1998). To obtain information on perceived economic status, a woman was asked whether she considered her household's economic situation to have been always in deficit, occasionally deficit, balanced or surplus in the preceding year. A household was categorized as 'deficit' if she answered either always deficit or occasionally deficit. A

SES score was constructed using a combination of the three SES indicators. The score ranged from 0 to 3 based on the accumulated number of positive attributes. For example, a woman who reported that she had formal schooling, was economically non-deficit, and had more than 0.5 acre of land, was given a SES score of 3.

Biochemical analysis

From a drop of venous blood sample Hb concentration was determined by use of HemoCue® system. The HemoCue method has been shown to be comparable in accuracy and precission with the standard cyanmethemoglobin method (John and Lewis, 1989). The accuracy of the HemoCue® machines was checked daily using control cuvettes provided with the machines. Hb concentration <110 g/L was defined as anemia, 100-109 g/L as mild anemia, 70-99 g/L as moderate anemia and <70 g/L as severe anemia (WHO 1998).

Venous blood was collected in an untreated evacuated tube and within 4 hours transported on ice to the field laboratory. After centrifugation, serum was taken off and frozen at -20°C. The frozen samples were transported on dry ice to the ICDDR,B laboratory in Dhaka and stored at -70°C. Analysis of the serum samples was performed at the end of the study at the Department of Nutrition, University of California, Davis. SF was assessed using immuno-radiometric assay (R & D Systems, Minneapolis, MN, USA). SF values < 12 μg/L were considered to reflect depleted iron stores (Institute of Medicine 1990). Soluble sTfR were assessed by an enzyme immunoassay double sandwich method (Ramco Laboratories, Houston) (Flowers 1989). sTfR Values > 8.5 mg/L were indicative of tissue iron deficiency (Carriaga 1991).

Stool samples were collected on the same day of blood sampling from all participating women to detect ascaris and hookworm infestations by microscopic examinations. The sample was diluted in sodium chloride solution and the presence of worms was evaluated by a semi-quantitative technique (Brooks 1995).

Statistical analysis

Data entry and analysis were done by use of SPSS for Windows software package (version 7.5.1). Logarithmic transformation was performed and nonparametric statistical methods were used when data were not normally distributed (SF, sTfR and sTfR/SF). To detect difference between two independent groups, Student's *t* test was used. Chi square test was used to test the association between categorical variables.

Results

The mean Hb concentration was equal to the cut-off for anemia according to the set criteria of WHO (Table 1). Median Hb was somewhat lower, 109 g/L. As expected, both STfR and SF had skewed distribution. Median sTfR was 6.2 mg/L and median SF was 13.7 μg/L. The cumulative distributions of Hb, sTfR and SF are shown (Figure 1-3).

Half of the women were anemic (Table 2). Most of the anemia was mild or moderate and none of the women was severely anemic. The prevalence of iron deficiency ranged from 24% to 54%, depending on the indicator used. The prevalence of IDA ranged from 15% to 33%. The lowest prevalence of IDA was estimated when high sTfR was used as an indicator.

Among the anemic women, the prevalence of high sTfR was 31%, low SF was 56% and iron deficiency (high sTfR and/or low SF) was 66%. Among the non-anemic women the corresponding estimates were high sTfR 19%, low ferritin 31% and iron deficiency 42%.

Participating and non-participating women did not statistically differ in terms of age, gestational age, family size and SES score (Table 3). However, participating women had fewer children than non-participants and there was a small difference in terms BRAC membership (p=0.07). There were no significant difference in anemia and IDA prevalence associated with BRAC membership (p=0.82 and 0.81). Parity had no significant association with anemia prevalence (p=0.82) but was significantly associated with the prevalence of IDA (p= 0.04). Although no statistically significant association was found a tendency of lower anemia and IDA prevalence among women with higher SES score (p=0.14 and 0.17, respectively)

Discussion

The prevalence of anemia among these pregnant rural Bangladeshi women was 50%. Despite this high prevalence none of the women had severe anemia. More than half of the women had iron deficiency defined as either depleted stores (low SF) or tissue iron deficiency (high sTfR), and up to 33% of the women had IDA.

The prevalence of anemia in our study is within the range previously reported from Bangladesh (HKI 1999, INFS 1966, 1976, 1983, Jahan 1998). The prevalence can be compared to information from India, where a national estimate among pregnant women is 87% (ICMR 1989). Smaller studies representing different geographical areas in India show a considerable variation (between 51% and 88%) (Mathan 1979, Seshadri 1998, Rusia 1999). A prevalence of 53% has been reported from Nepal (Stolzfus 1999) and in Sri Lanka 65% (Atukorala 1994). A lower prevalence has been found (33%) among pregnant women in an urban low-income community in Pakistan (Aziz-Karim 1990). With the possible exception of India the anemia prevalence found in Bangladesh is of similar magnitude of what is reported from the neighboring countries.

A prevalence of anemia above 30% is considered sufficiently high to "trigger" routine iron supplementation of pregnant women (WHO/UNICEF/UNU 1998). When the prevalence exceeds 40% the supplementation period should be prolonged and continue 3 months post partum (Stolzfus et al 1997). It is clear that the anemia prevalence in Bangladesh fall in the latter category.

Despite an overall high prevalence, none of the participating women had severe anemia. A large variation is seen in the prevalence of severe anemia among pregnant women in South Asian region. In India the national estimate of severe anemia is 13% (ICMR 1989), but selected studies report up to 27% in an area where overall anemia was 88% (Krishnaswamy 1998). In Nepal 3% of the pregnant women have been reported to be severely anemic (all anemia 53%) (Stolzfus 1999). Despite many similarities between India and Bangladesh it seems that the prevalence of severe anemia is lower in Bangladesh. Hookworm, malaria and HIV infections are known to be associated with high prevalence of severe anemia (Olukoya 1991, Brabin 1990, McDermott 1996). These factors are not common in Bangladesh and may explain the lack of severe anemia. The large variation in prevalence and severity of anemia in the South Asian region may reflect differences in epidemiology of factors contributing to anemia and its severity.

It is still not clear to what extent different levels of severity of anemia is associated with maternal morbidity/mortality and poor pregnancy outcome. Even if a more sever anemia is associated with an increased risk of negative outcome the attributable proportion of a health problem may still be lower due to a larger number of women having mild or moderate anemia.

There is no globally agreed single criterion to define iron deficiency. Interpretation of indicators of iron status is particularly difficult during pregnancy because most of the commonly used indicators are altered by gestation due to increase in plasma volume and red cell mass independent of iron status (Cook 1989, DeMaeyer 1989). In settings like Bangladesh where infections and inflammatory diseases are common, further difficulties are added as some of the indicators are affected by these conditions (Baynes 1996, Lipschitz, 1990, Olivares 1995).

To our knowledge there is no published information on SF concentrations among pregnant women in Bangladesh. Data on SF are also limited in other South Asian countries. In Sri Lanka the mean SF concentration was 16 µg/L (low SF 57%)

(Atukorala 1994, Goonewardene 1995) and in Pakistan 16 μg/L (low SF 55%) (Hamedani 1991). A study done among pregnant women in India showed that among <u>non-anemic</u> women mean SF concentration was 27 μg/L (low SF 15%) (Rusia 1999). Pregnant women of poor SES background in the USA were found to have a similar proportion of low SF (44%) (Carriaga 1991) as was observed in Bangladesh. All of these prevalence of low SF are considerable larger than among pregnant women coming from a presumably well-nourished population in Sweden (median, 34 μg/L; low SF10%) (Åkesson 1998).

The information on sTfR concentration is even more limited in South Asian region. A study done among Indian pregnant population reported data on sTfR, but the information was difficult to interpret as it was stratified according to the women being anemic or not (Rusia 1999). Among <u>non-anemic</u> women 41% had high sTfR and in the <u>anemic</u> women as many as 86% were reported to have high sTfR (Rusia 1999). To our knowledge, information on sTfR among pregnant women in any other countries of this region is not available. Swedish women pregnant in their first semester had median sTfR of 4.1 mg/L (high sTfR 11%) (Åkesson 1998) and pregnant women of low SES in USA had median sTfR 5.96 mg/L (high sTfR 10%) (Carriaga 1991).

In our study about one-third (29%) of the pregnant women had depleted iron stores without an indication of tissue iron deficiency. This indicates that many pregnant women had absent iron stores but necessarily not iron-deficient erythropoiesis, which is in agreement with findings reported among pregnant women of low SES in the USA (Carriaga 1991).

Twelve percent of the women showed normal iron stores but with signs of tissue iron deficiency. Serum ferritin is known to rise in the presence of infections even in iron deficient subjects (Olivares 1995). However, in our study no information on infections were collected and it is not known whether these women had elevated SF due to infection.

Despite the high prevalence of iron deficiency (24-54%) none of the women had severe anemia. This suggest that iron deficiency is not associated with sever anemia or that the severity of iron deficiency in this population was not sufficient to produce severe anemia.

To design an appropriate intervention for controlling and preventing anemia it is important to know the contribution of iron deficiency. But, measurement of iron deficiency is not straightforward and a valid tool for its assessment is still debatable. The two indicators of iron deficiency such as sTfR and SF provide different pieces of information and there is no general agreement on which of them is more appropriate for classifying IDA. Thus in this study the prevalence of IDA was presented using either one of the indicators or both of them. Depending on the criteria used the IDA ranged from 15-33%. There is a wide range of prevalence estimate of IDA, limiting the practical usefulness of a definition of IDA based on these indicators. However, an approach that may be more useful is to evaluate response to iron supplementation by increase in Hb concentration. Further research is needed in different settings to have an agreed definition of IDA.

The data was drawn from women participating in community-based ANCCs. The sampled and non-sampled women were found to have similar characteristics in terms of age, gestational age and family size (Table 3). Although not statistically significant, the sampled women seemed to have better SES (p=0.15) and parity was significantly lower. SES and parity are generally known to be associated with anemia prevalence. In our study population parity was not associated with anemia (p=0.49). However, it was positively associated with iron deficiency and thus IDA (p<0.01). Thus, the conclusion is that while the estimate of anemia is representative of pregnant women in the area, the prevalence of iron deficiency and IDA were possibly underestimated due to higher participation of women with low parity in the study.

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TABLE 1
Hemoglobin and indicators of iron status of participating women (n=215)

	Mean±SD	95% CI
Hemoglobin (g/L)	110±14	108-112
sTfR (mg/L)	7.0±4.3	6.4-7.6
Log sTfR[1]	0.79±0.22	0.76-0.82
Serum ferritin (μg/L)	21.5±23.7	12.6-19.8
Log SF	1.06±0.56	0.99-1.13
sTfR/SF	1605±2725	1283-1963
Log sTfR/SF	2.73±0.65	2.6-2.8

sTfR – Serum transferrin receptor; sTfR/SF – Ratio of sTfR and SF,
CI - Confidence interval

FIG 1. Cumulative distribution of hemoglobin concentration among study women in Mymensingh, Bangladesh

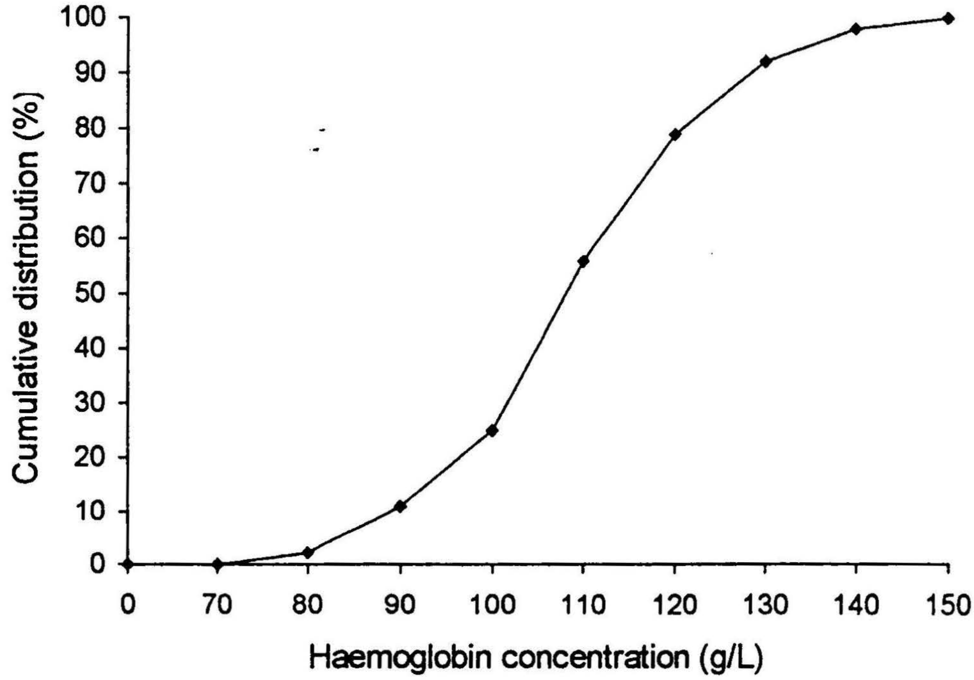

FIG 2. Cumulative distribution of sTfR concentration among study women in Mymensingh, Bangladesh

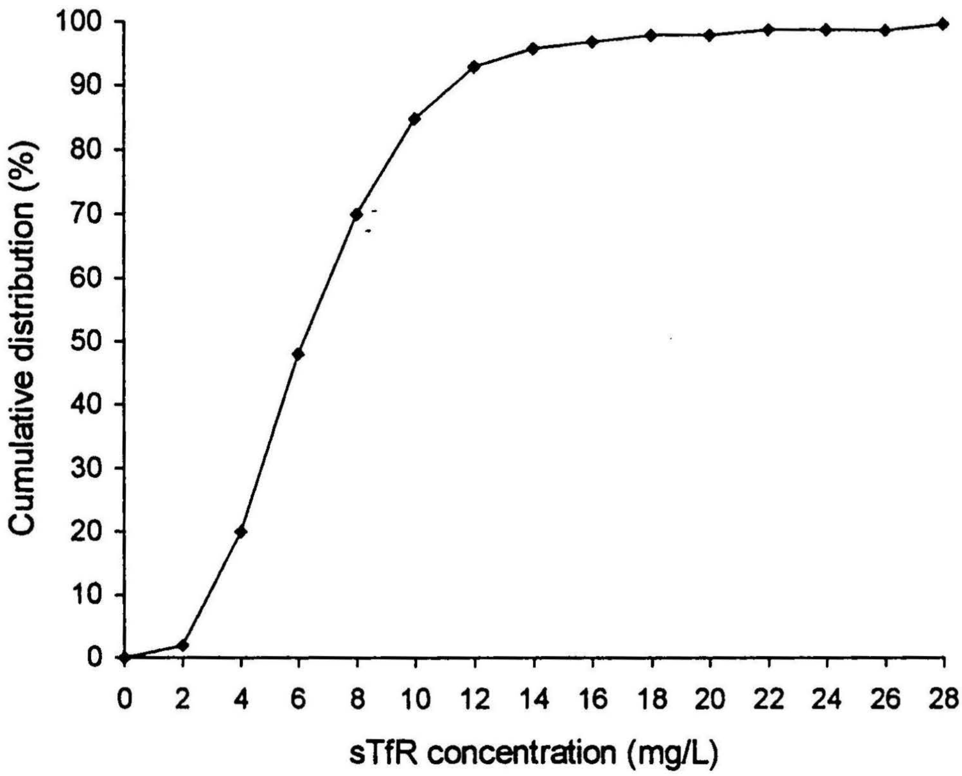

FIG 3. Cumulative distribution of serum ferritin concentration among study women in Mymensingh, Bangladesh

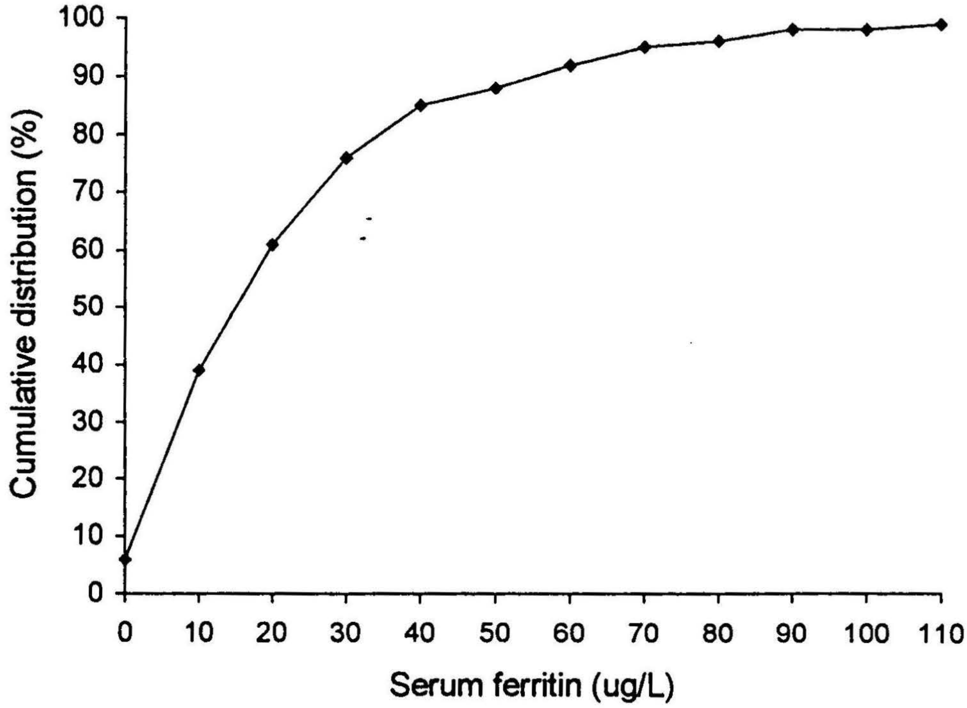

TABLE 2
Prevalence of anemia, iron deficiency and iron deficiency anemia among participating women in a rural area of Mymensingh, Bangladesh

	All women (n=215)	95% CI
Anemia (%)		
All (<110 g/L)	50	44-58
Mild (100-<110 g/L)	28	
Moderate (70-<100 g/L)	23	
Severe (<70 g/L)	0	
Iron deficiency (%)		
sTfR >8.5 mg/L	24	19-31
SF <12 μg/L	42	35-49
sTfR/SF >500	48	41-55
sTfR >8.5 mg/L and/or SF <12 μg/L	54	47-61
Iron deficiency anemia (%)		
Hb <110 g/L & sTfR >8.5 mg/L	15	11-21
Hb <110 g/L & SF <12 μg/L	28	22-34
Hb <110 g/L & sTfR/SF >500	32	26-38
Hb <110 g/L & (sTfR>8.5 and/or SF <12)	33	27-39

TABLE 3
Comparison of biological and socio-economic characteristics of pregnant women in a rural area of Mymensingh, Bangladesh

	Sampled women (n=215)	Non-sampled women (n=396)	p^1
Age (yr)[2]	24.2±6.0	24.3±5.8	0.84[3]
Gestational age (wk)[2]	18.4±4.6	17.9±5.8	0.58[3]
Parity[2]	1.8±1.8	2.2±2.0	0.05[3]
Family size[2]	4.6±2.3	4.7±2.3	0.50[3]
SES	1.19+0.74	1.06+0.75	0.15[3]
BRAC membership (%)	9	14	0.07[4]
Presence of hookworm (%)	1	-	-
Presence of ascaris (%)	39	-	-

[1]Significance of difference between participating and non-participating women
[2]mean±sd
[3]Student's *t* test
[4]Chi-square