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Cluster and regional level variation of hemoglobin concentration of ever-married women in Bangladesh: a linear mixed model approach

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Abstract

Background: The hemoglobin protein plays an essential role in health and development in the human body. Women with inadequate Hb levels develop anemia. In light of the regional heterogeneity in Bangladesh, the aim of this study is to identify the risk factors associated with low Hb concentration in ever-married women.

Methods: The study extracted data from the Bangladesh Demographic Health Surveys (BDHS) conducted in 2011. Since the hemoglobin level was not measured in BDHS 2014 and BDHS 2017, the study used BDHS 2011. A total of 5,699 ever-married women aged (15-49) years were used in the study. Both descriptive and inferential statistics applied to answer the research questions. Multilevel linear mixed effect modelling was applied to identify the risk factors of hemoglobin level at different hierarchical levels simultaneously and the different level variations were observed.

Results: The average age of women was 31 years with standard deviation of 9.33 years. The mean (SD) of hemoglobin level of women was 120.95 (13.81) g/L. The highest mean (SD) level of hemoglobin was found in the Khulna 122.48 (13.26) g/L and the lowest in the Barisal 119.61 (13.21) g/L. The multilevel model resulted that using the contraceptive method, pregnant women, married women, breastfeeding mother, age of mother, body mass index, and total children ever born had significant effect on the low hemoglobin level.

Conclusion: Analyzing the individual, cluster, and regional influence, the current study determined the most relevant socioeconomic, demographic, and environmental risk factors for low hemoglobin levels of women in Bangladesh.

Keywords: anemia, BDHS, cluster, hemoglobin, multilevel

Abbreviations: BDHS, Bangladesh demographic health survey; LMM, linear mixed model; MLE, maximum likelihood estimation; REML, restricted maximum likelihood; AIC, Akaike's information criterion; AICc, corrected Akaike information criterion; BIC, bayesian information criterion; ICC, intra-unit correlation or intra-cluster correlation

Introduction

In order to sustain and repair itself, each of the billion cells in the body needs oxygen. Hemoglobin assists red blood cells in developing their disc-like shape, which allows them to pass more easily through blood vessels. Blood tests are used to determine hemoglobin levels, which are often represented in grams per deciliter (g/dL) of blood. A hemoglobin level below normally indicates anemia. For men, the normal hemoglobin concentration range is 135 to 175 g/L and for women, 120 to 155 g/L. Children's hemoglobin ranges vary based on age and sex.[1,2] High hemoglobin levels may be causing polycythemia, a rare blood disease that causes serious illnesses like heart attacks, strokes, and clots. Low hemoglobin levels typically diagnose anemia.

According to WHO, 48.8% of the world's population is anemic, with significant regional and population group differences.[2] Due to a woman's increased need for blood supply during pregnancy and menstrual blood loss, women who are of childbearing age are especially vulnerable to iron deficiency anemia. Inadequate diet and other medical factors may increase the risk of anemia in older persons.

Many women in underdeveloped nations get iron deficiency anemia, especially in the years leading up to childbirth. The main identifying feature of iron deficiency anemia is homogeneous intentness.[3] Anemia is the most common nutrient deficiency in pregnant women around the world. It causes 20% of all maternal deaths worldwide[4–6] and affects nearly one-third of the world's population.[7] Almost 1 billion people in the world are affected by iron -deficiency anemia.[8] About 1,83,000 people died due to iron deficiency anemia in 2013, whereas in 1990, the situation was 2,13,000.[9]

Anemia is considered to be a major public health issue in Bangladesh among women and children.[10] To figure out the prevalence of anemia, the hemoglobin level of children and ever-married women aged (15–49) was assessed for the first time during the 2011 Bangladesh Demographic Health Survey (BDHS).[11] The prevalence of anemia among women aged (15-49) was 39.9% in 2016, with the highest value over the previous 26 years being 55.3% in 1990 and the lowest value 39.7% in 2014.[12] In rural areas, anemia was 43% among adolescent girls, 45% among non-pregnant women, and 49% among pregnant women.[13]

Most of the studies in Bangladesh have been done cross-sectionally. Those studies ignore the hierarchical structure of the data and have determined the risk factors in women with low hemoglobin levels. However, none have been performed collectively on identifying the risk factors of low hemoglobin concentration or anemia. Therefore, our goal is to highlight the risk factors for low hemoglobin levels, emphasizing the significance of socioeconomic factors, physical factors, behavioral factors, environmental factors, and health facilities, considering the multilevel clustering structure. To the best of our knowledge, this is the first large-scale study on Bangladeshi women's hemoglobin (Hb) levels.

Materials and methods

Study population

Data on the hemoglobin levels of women (15-49 years) were collected from the Bangladesh Demographic Health Surveys (BDHS). The most current survey was the 2017 BDHS; however, because hemoglobin level was not measured sequentially in the 2014 and 2017 BDHS, we used data from the 2011 BDHS. A two-stage stratified sampling design (20 strata, 600 EAs, 30 households per EA) was used to conduct the BDHS 2011 survey, which included all divisions (regions) and districts. The data set included 17,141 households and 17,842 ever-married women aged (15-49) years.[11] In total, 5,699 women have had information on their hemoglobin levels.

Dependent variables

The hemoglobin level was a continuous response/outcome variable throughout the study. The hemoglobin level was measured in grams per liter (g/L).[11]

Independent variables

This study included socioeconomic, demographic, and household information. The association with hemoglobin level was studied using several explanatory variables or risk factors. All variables were recorded at the individual/household, cluster, and regional levels. Following the previous studies, several predictors such as place of residence, religion, household wealth status, husbands' education, and women's education, women's age at birth, and women's exposure to mass media associates, access piped water and sanitary toilet, BMI, total children ever born, currently marital status, currently pregnant, currently breastfeeding, currently, contraceptive method, menstrual period with the outcomes were considered in this study.[1,14,15]

Statistical analysis

Descriptive statistics was used to describe the basic and socio-demographic characteristics. The mean and standard deviation was used for continuous variables, and the frequency table with percentages was used to describe categorical variables. The multilevel modeling approach was used to identify the risk factors. Multilevel Linear Mixed Model (LMM) is a powerful statistical modeling technique that includes explanatory variables at several levels of the hierarchy.[16–18] Three-level LMM was used to investigate the relationships between predictors and hemoglobin levels, considering the clustering of individuals/women within clusters and regions (divisions).[19]

Suppose Y_{ijl} was the hemoglobin level (continuous response variable) for the l^{th} women belong to j^{th} cluster of the i^{th} region. It was assumed that the index follows a three-level model as below:

$$Y_{ijl} = X_{ijl}^{T}\beta + \eta_i + \mu_{ij} + \varepsilon_{ijl} \text{ -----(1)}$$

where,

X_{ijl}^{T} =vector of explanatory information

β =vector of the regression parameter

η_i =region/division -specific random effect

μ_{ij} =cluster -specific random effect

ε_{ijl} =mother -specific random effect

It was assumed that the level specific random effects were identically and independently distributed with mean zero and homoscedastic random effect variances $\sigma_{\eta}^{2}(region)$ $\sigma_{\mu}^{2}(cluster)$ and $\sigma_{\varepsilon}^{2}(residual)$ respectively.[20]

The parameters were estimated using the Restricted Maximum Likelihood (REML) procedure. Unlike maximum likelihood estimation (MLE), REML produced unbiased estimates of variance and covariance parameters of a linear model.[21] The likelihood ratio-based Type 3 test was used to assess the risk factors for the mother's low hemoglobin concentration. The Type 3 test of a predictor of interest is the joint test that the parameters associated with a predictor are zero.[20] The individual predictor for which p-values were less than 0.10 in the univariate analysis was chosen as the candidate predictor for the full model. Several selection criteria were considered for selecting the best model for the response variable. For selecting the best model, different types of information criteria, such as the lowest value of Akaike's information criterion (AIC), Corrected Akaike Information Criterion (AICc), Bayesian Information Criterion (BIC), Likelihood Ratio Test (LRT), were considered. From the model, we showed that the correlation between two mothers in the same cluster which was known as the intra-unit correlation or intra-cluster correlation (ICC). The calculation for each specific level ICC is the following:

$$ICC(region) = \frac{(\sigma_{\eta}^{2}(region))}{\sigma_{\eta}^{2}(region) + \sigma_{\mu}^{2}(cluster) + \sigma_{\varepsilon}^{2}(residual)}$$

$$ICC(cluster) = \frac{\sigma_{\eta}^{2}(region) + \sigma_{\mu}^{2}(cluster)}{\sigma_{\eta}^{2}(region) + \sigma_{\mu}^{2}(cluster) + \sigma_{\varepsilon}^{2}(residual)}$$

The ICC was used initially to determine whether multilevel analysis was even necessary for the data. The value of ICC ranges from 0 to 1. If the ICC is 0, observations within clusters are not similar to observations from different clusters, and if the ICC is greater than 0, a multilevel regression model is appropriate for the analysis.[22] Considering the cluster effect, three levels of linear mixed model analysis were used for examining the association between hemoglobin level and socioeconomic, demographic and environmental factors. Finally, a full model was fitted using all candidate variables, and a backward elimination procedure was applied to select the ultimate risk factors that were significant at $p < 0.05$. All analyses were done using two-tailed tests at a 5% significance level. The statistical analyses were performed using R version 4.1.3.

Results

The dataset included information on 5,699 women aged (15-49) years. The mean hemoglobin level was 120.95 g/L with a standard deviation (SD) of 13.81 g/L. Results showed that there was a significant variation in hemoglobin levels by geographical region in Bangladesh. Figure 1 shows the mean hemoglobin level of women by regional geographical areas (division). The highest mean hemoglobin level was observed in the Khulna region, at 122.48 g/L, and the lowest was in Barisal, at 119.61 g/L.

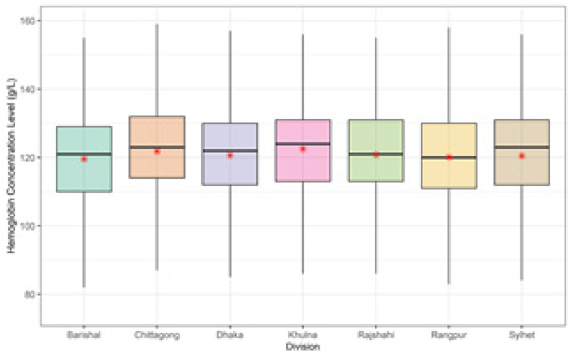

Figure 1 Box-plot of hemoglobin level of women aged (15-49) years by division.

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The basic and socio-demographic characteristics of women are described in Table 1. The average age of women was 31 years with standard deviation of 9.33 years. The median number of ever born children of women was 2 with interquartile range of 3. Most women lived in rural places (65.33%), 19.02% of women belonged to the middle-class household wealth index, and 36.08% of women went to Secondary school. Approximately 25% and 5% of women were currently breastfeeding and had currently amenorrheic, respectively. Almost 58% of women had their regular menstrual period cycle. About 89% of women had accessed to piped water and 57% had sanitary toilet facilities (Table 1).

Table 1 Characteristics of women aged 15-49 years

Variables	% (n)
Place of residence	
Urban	34.67(1976)
Rural	65.33(3723)
Marital Status	
No	6.21 (354)
Yes	93.79(5345)
Wealth index	
Poor	36.36(2072)
Middle	19.02(1084)
Rich	44.62(2543)
Literacy	
No	35.49(2021)
Yes	64.51(3674)
Highest education level	
Illiterate	25.62(1460)
Primary	30.81(1756)
Secondary	36.08(2056)
Higher	7.49 (427)
Currently pregnant	
No or Unsure	93.74(5342)
Yes	6.26 (357)
Currently breastfeeding	
No	75.07(4278)
Yes	24.93(1421)
Currently amenorrheic	
No	94.88(5407)
Yes	5.12 (292)
Current contraceptive method	
Not Using	42.20(2405)
Pill	25.48(1452)
IUD	0.79 (45)
Others	31.53(1797)
Menstrual period	
Regular cycle (last menstruation max. 6 weeks ago)	57.97(3303)
Last time 6 weeks to 6 months ago	22.31(1271)
Last time to 6 months to 1 year ago	4.93 (281)
More than 1 year ago	2.98 (170)
In menopause/hysterectomy	6.83 (389)
Before last birth	4.98 (284)
Access to piped water	
No	89.10 (5078)
Yes	10.90 (621)
Access to sanitary toilet	
No	42.92 (2446)
Yes	57.08 (3253)

The risk factor associated with low hemoglobin level

At first, the full multilevel LMM was fitted using the candidate risk factors. The candidate risk factors were identified using the univariate LMM. Secondly, the backward elimination procedure was used to build up the model to determine the important risk factors, considering the correlation of cluster-specific effects (level-2), and region-specific (division) effects (level-3). Finally, the summary statistics of the fitted models was calculated. Table 2 indicates the 3-level model (denoted by 3L.R.C) and 2-level model (denoted by 2L.C) in terms of the AICc, BIC and likelihood ratio test. In all cases, 3-level model showed the better performer model. The ICCs of women were found to be 0.004 at the 2-level model (at cluster) and 0.092 at the 3-level model (at region). The 3L.R.C model provided a greater ICC compared to other multilevel models. Therefore, the 3L.R.C model was considered the best one in this study (Table 2).

The factors associated with low hemoglobin levels were investigated using three levels of clustering effects. Table 3 shows the risk factors which are associated with low hemoglobin level. It was observed that the hemoglobin level of women declined by about 9 percent with increasing age $(p < 0.001)$.Women's hemoglobin levels dropped during pregnancy. BMI had a low positive effect on hemoglobin levels. Women who last menstruated six weeks to a year ago had lower hemoglobin levels than women who had a regular cycle (of up to 42 days). Hemoglobin levels were significantly higher in women who had undergone a hysterectomy, experienced menopause, or had their last period more than a year ago and had never menstruated. Women who were currently breastfeeding $(estimate: -1.65; p < 0.001)$ and amenorrheic $(estimate: -6.33; p < 0.001)$ had a lower hemoglobin level compared to women who were not breastfeeding and amenorrheic. It was also noted that the total number of children ever born $(estimate: -0.34; p = 0.01)$ to a woman had a negative effect on hemoglobin levels. It was predicted that having more children reduced a woman's hemoglobin level by 0.34 $(p < 0.001)$ units. Having received higher education had a highly positive effect on hemoglobin levels. The women who were higher educated had better hemoglobin levels $(estimate: 0.97, p < 0.001)$ than those with no education. Otherwise, women who received primary and secondary education had a lower hemoglobin level. Women who used pills $(estimate: 3.03, p < 0.001)$ and other contraceptive methods $(estimate: 0.45, p < 0.001)$ other than intrauterine device (IUD) had a positive impact on their hemoglobin level compared to those who never used contraceptives (Table 3).

Discussion

This study investigated the risk factors for low hemoglobin levels in women in Bangladesh. The effects of various factors on women's hemoglobin concentrations at the individual, cluster, and regional levels were investigated simultaneously. Cluster and region-specific random effects were also investigated to reveal variation in cluster and regional level outcomes. In this study, it was found that pregnant women had lower hemoglobin levels. Another finding from a recent study revealed that pregnant women's hemoglobin levels dropped during their pregnancy, which was a well-known physiological event.[23,24] Malawi DHS also reported lower hemoglobin levels among pregnant women.[1] It was also found that women who were breastfeeding and had amenorrhea had lower hemoglobin levels than women who were not breastfeeding and had amenorrhea. This was thought to be mostly due to the fact that women need more nutrients when they were breastfeeding. This finding was consistent with other studies.[23,25] Previous research found that the prevalence of anemia was higher in women who were currently breastfeeding (45.9%) or had amenorrhea than in women who were not breastfeeding (39.7%) or did not have amenorrhea.[14] This finding might also partially explain why women with higher parity were more likely to have low hemoglobin levels. Multiple periods of breastfeeding (from successive children) would tend to diminish the health status of higher-parity mothers, although there might be other contributing factors. According to Haverkate et al,[23] married women had a positive association with hemoglobin levels, however, this was not found to be significant in our study. A positive association between hemoglobin levels and BMI was revealed, which supported with previous findings.[14,15] In addition, hemoglobin levels decreased with age and the total number of children born, which were consistent with previous research.[26–28] We discovered significant geographical differences despite investigating the risk factors for women's hemoglobin levels. This was why the factors could be related to the location of the household and may indicate geographical differences in factors related to hemoglobin levels in women.

Table 2 Summary statistics of the fitted multilevel model for hemoglobin

Model	df	Random-effects parameters			BIC	AICC	ICC
		σ_η^2 (region-level)	σ_μ^2 (cluster-level)	σ_ε^2 (residual)			
2L.C	26	0.693	-	172.34	45541	45368	0.004
3L.R.C	27	0.631	14.071	158.63	45438	45258	0.092
LR test of $H_0 : \sigma_\mu^2 = 0$,	$\chi^2 = 111.91$,	$p < 0.001$	2L.C vs 3L.C.R				

Table 3 Parameter estimates using multilevel LMM considering women at level-1, cluster at level-2, and region at level-3

Variables	**Estimate**	**P-value**
Intercept	114.3 (1.5)	<0.001
Marital Status		
No*	…	…
Yes	-0.44 (0.7)	0.56
Wealth index		
Poor*		
Middle	0.32 (0.5)	0.53
Rich	0.91 (0.5)	0.07
Literacy		
No*	…	…
Yes	0.95 (0.6)	0.13
Highest educational level		
No education*		
Primary	-0.52 (0.6)	0.41
Secondary	-0.15 (0.8)	0.84
Higher	-0.84 (1.0)	0.41
Currently pregnant		
No or unsure*	…	…
Yes	-13.3 (0.8)	<0.001
Currently breastfeeding		
No*	…	…
Yes	-1.65 (0.5)	<0.001
Currently amenorrheic		
No*	…	…
Yes	-6.33 (1.9)	<0.001
Contraceptive method		
Not using*	…	…
Pill	3.03 (0.5)	<0.001
IUD	-2.56 (1.9)	0.19
Others	1.27 (0.5)	<0.001
Menstrual period		
Regular cycle*	…	…
Six weeks to 6 months ago	1.80 (0.5)	<0.001
Six months to 1 year ago	0.63 (0.8)	0.47
More than 1 year ago	2.33 (1.1)	0.02
In menopause/hysterectomy	1.07 (0.8)	0.17
Before last birth	3.54 (1.9)	0.06
Access to piped water		
No*	…	…
Yes	0.81 (0.6)	0.23

Table Continued...

Variables	Estimate	P-value
Access to sanitary toilet		
No*	…	…
Yes	-0.12 (0.5)	0.75
Mother age	-0.09 (0.01)	0.002
Body mass index	0.01 (0.001)	<0.001
Total children ever born	-0.34 (0.2)	0.01
Random Effect	Estimate	
Var (Division)	0.63	
Var (Cluster)	14.07	
Var (Error)	158.63	

Conclusions and recommendations

The current study identified the most important risk factors for low hemoglobin levels from the socioeconomic, demographic, and environmental perspectives considering the individual, cluster and regional effect. Using a multilevel model, it was illuminated that pregnant women, breastfeeding, amenorrhea, contraceptive method, menstrual period, age, BMI, and the total number of children ever born are the most significant determinants of low hemoglobin level in Bangladeshi women. It also explored the potential risk factors and multi-sectoral issues that were directly or indirectly related to low hemoglobin levels among women of reproductive age. Regarding the hemoglobin level, interregional differentials were observed. It is necessary to develop and implement short- and long-term plans and programs at national as well as subnational (divisions/regions) levels to eliminate the factors that are liable for low hemoglobin levels among women.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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